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Journal of the AMERICAN MEDICAL WOMEN'S ASSOCIATION

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VOLUME 6 | NOVEMBER, 1951 | NUMBER 11

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Woman's Medical Society of District of Columbia

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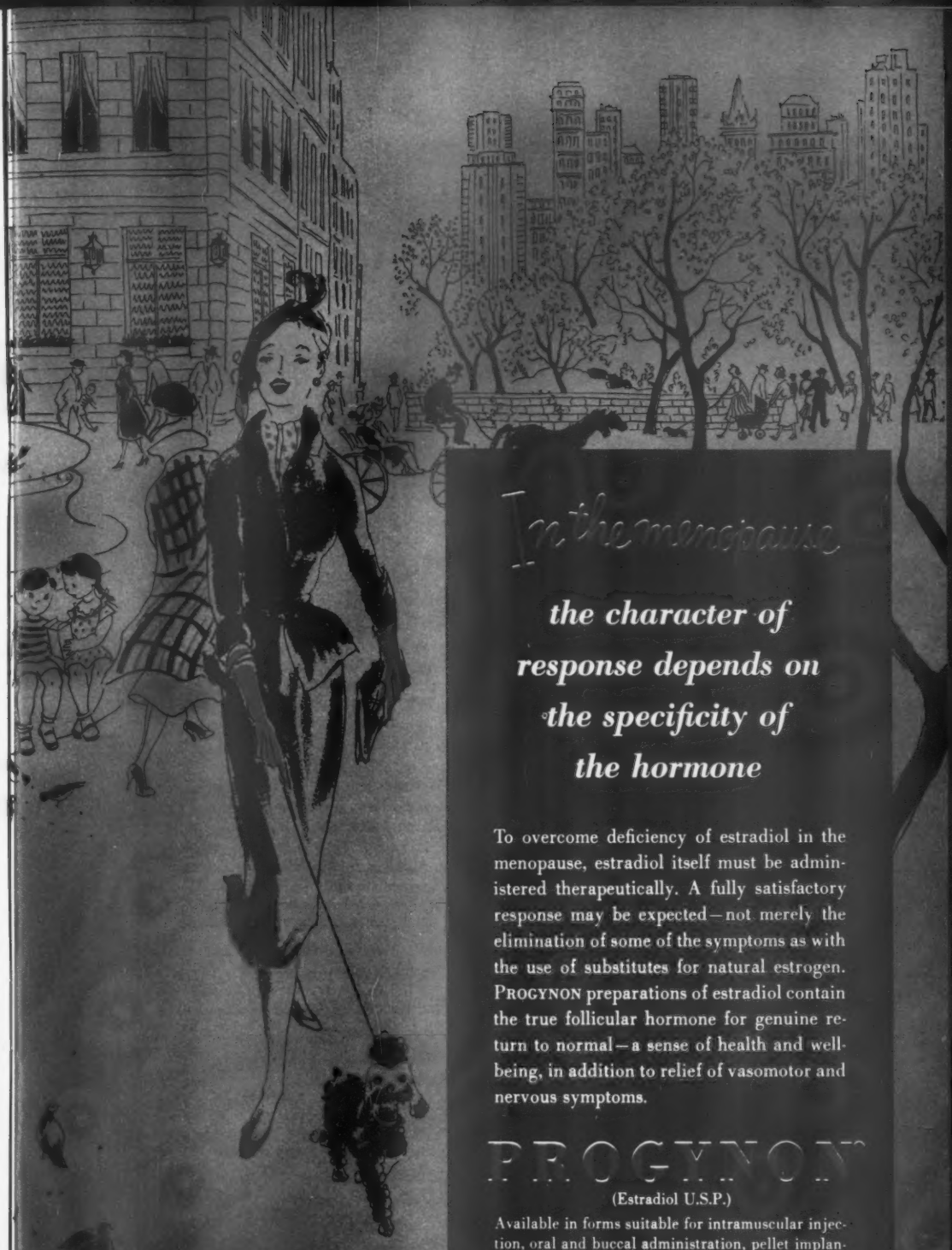

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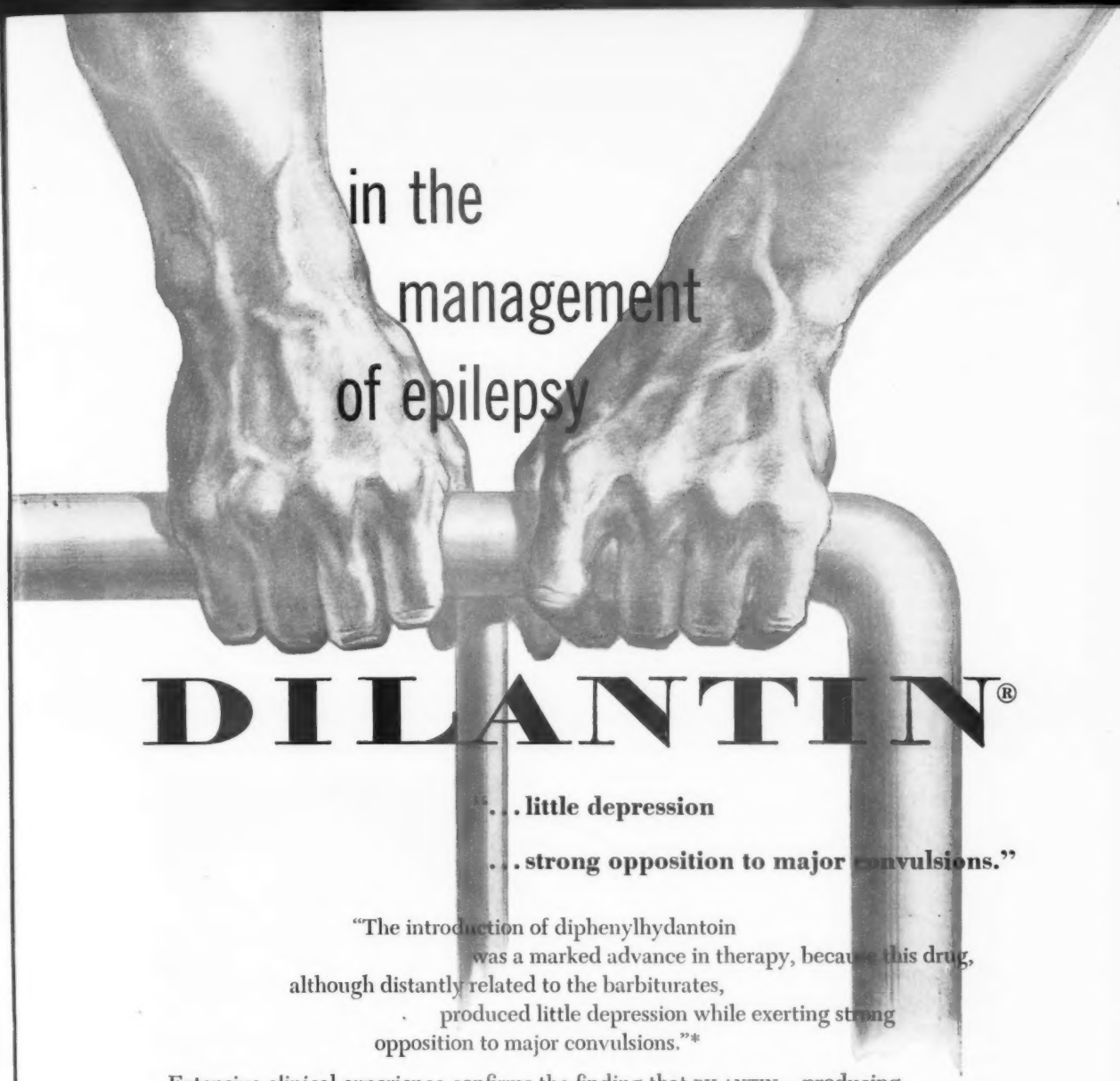

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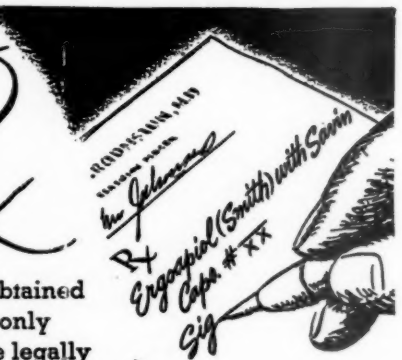

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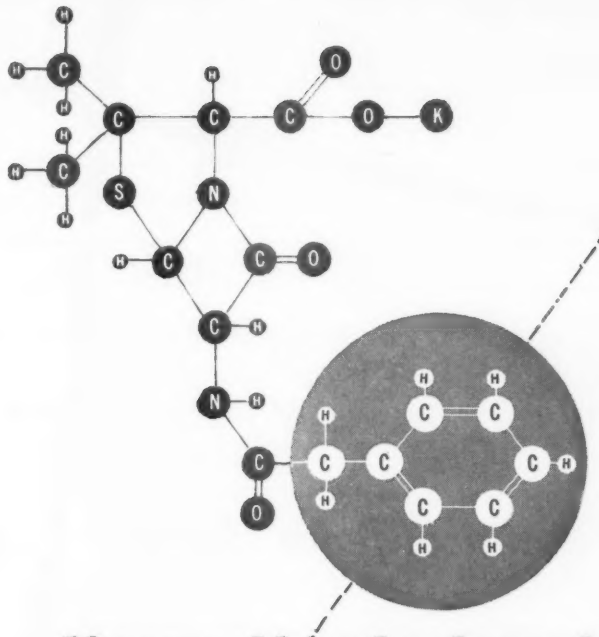

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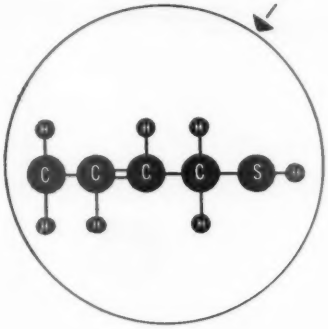

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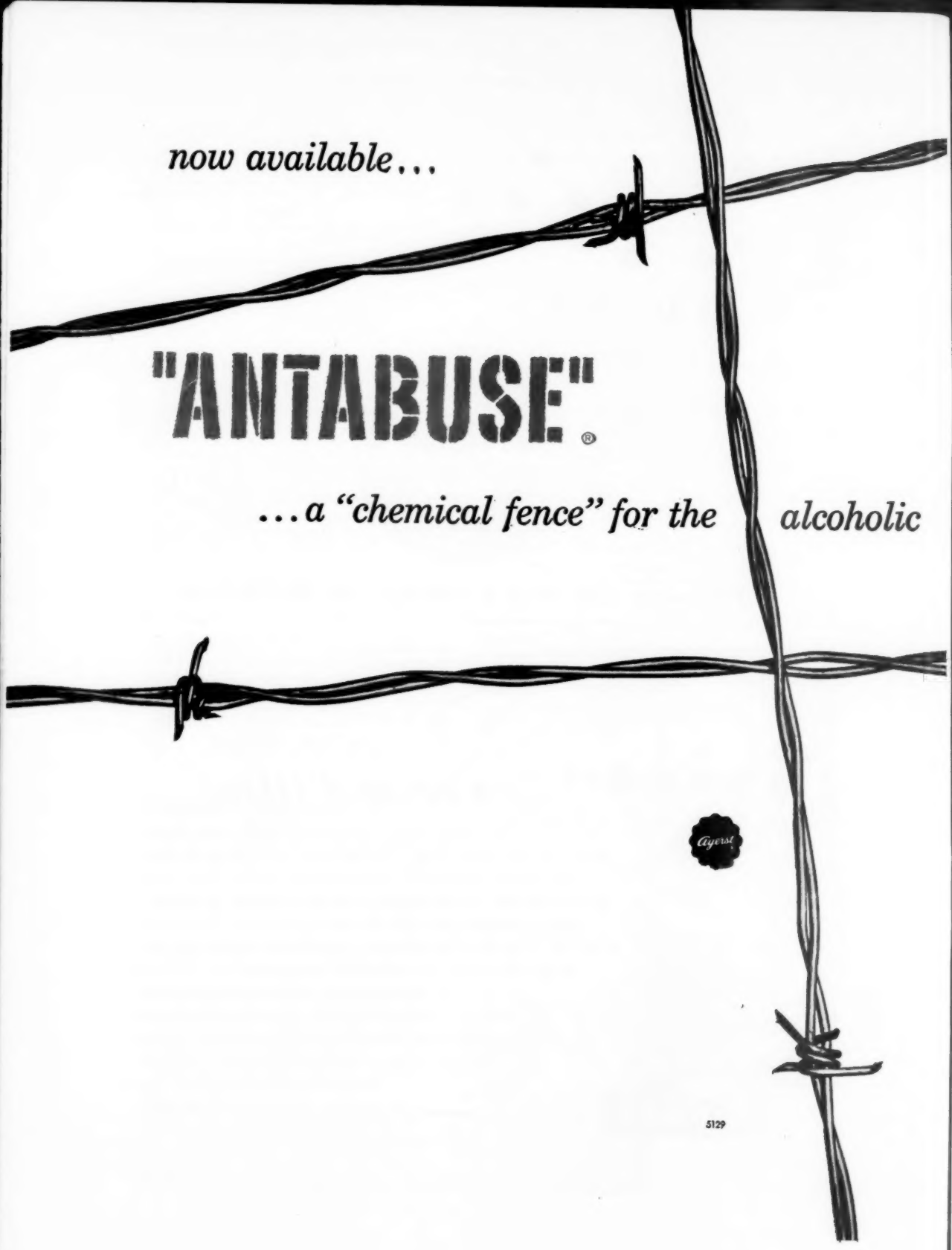

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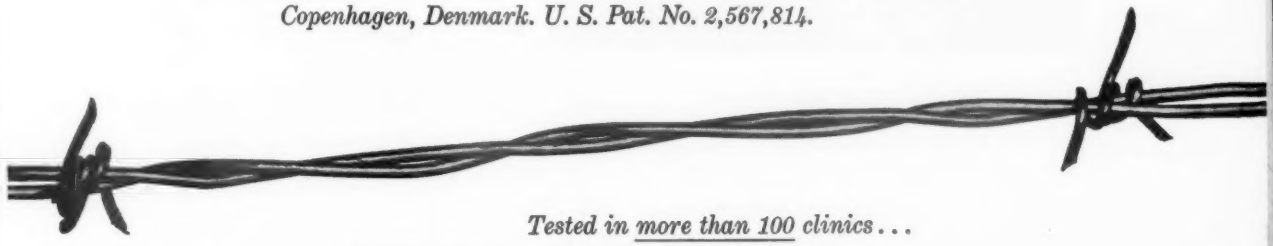

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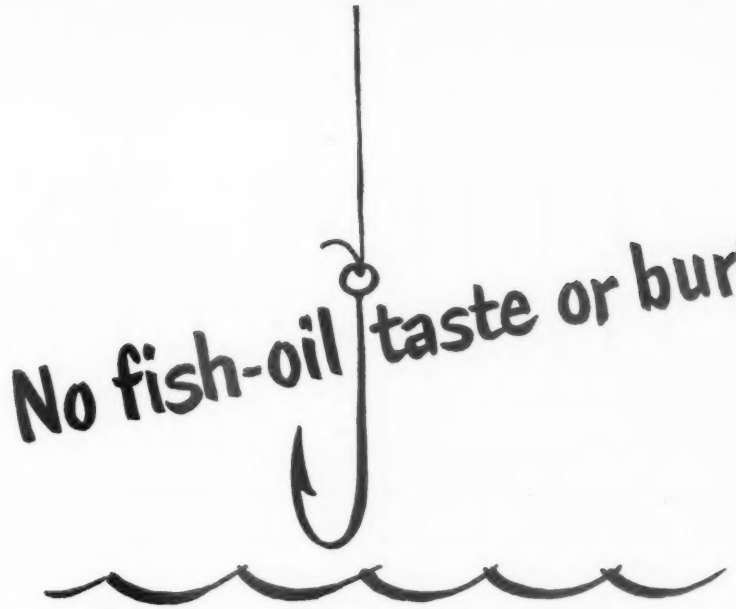

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1. Anspaugh, R. D.: Effects of Dexedrine Sulfate on Nausea and Vomiting of Pregnancy, Am. J. Obst. & Gynec. 60:888 (Oct.) 1950.

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Leukemia Research With Laboratory Mice

Thelma B. Dunn, M.D.

Leukemia is probably the most widely occurring of all the neoplastic diseases. It has been reported from a great variety of mammalian species, including many wild, domestic, and laboratory animals. It is of particular interest in the fowl, since it has been transmitted by a filtrable virus. This fact is of importance in fundamental cancer research, and many studies on the role of viruses in the etiology of cancer are based upon it. The study of leukemia in fowls is also of economic importance, since there is a serious loss to the poultry industry from leukemia. The manifestations of the disease in fowls differ in many ways from those in mammals, and there is doubt as to how close an identity this virus-related form may have to leukemia in man. There is, on the other hand, a great similarity between human leukemia and the disease as manifested in mice. Leukemia has been found in other laboratory animals, namely, guinea pigs and rats, but transmission in these animals is not often successful, since the same degree of inbreeding has not been attained as for mice and high leukemic strains have not been developed. In modern research on leukemia inbred strains of mice are usually employed and our present understanding of the disease is derived largely from these studies.

Dr. Dunn is Pathologist, Medical Officer, Hematology Unit in the Pathology Section, National Cancer Institute, United States Public Health Service.

Forms of Leukemia in Mice

In experimental research, the term leukemia is used in its broadest sense to denote any neoplastic process involving cells of the blood or blood-forming organs. The presence of leukemic cells in the blood stream is considered to be a more or less incidental feature of the disease and is not a requisite for diagnosis.

The forms of the disease now recognized in mice classified on the basis of cell origin are: lymphocytic; monocytic accompanying reticulum cell sarcoma; granulocytic; plasmacytic; and mast cell leukemia.

1. *Lymphocytic leukemia.* This is by far the most common type of leukemia in the mouse and nearly all of the research work in experimental leukemia has been done with this type. Enlargement of the thymus, lymph nodes, and spleen is a striking characteristic of lymphocytic leukemia; and these organs are packed with cells often resembling large lymphocytes. The neoplastic lymphocyte usually has a relatively large hyperchromatic nucleus and several prominent nucleoli. In some cases the cell may be so undifferentiated that its origin from the lymphocyte is doubtful. Hence, the precise identification of this form of leukemia in mice is as uncertain as the recognition of the cell of origin may be for acute undifferentiated leukemia of man. The malignant lymphocytes often appear in great numbers not only in the lymphoid tissues but in other organs (figure 1). Terminally a high leucocyte count may develop.

The incidence of lymphocytic leukemia is as high as 90 percent in one strain of mouse (strain C-58),

and there are other strains with a reasonably predictable high incidence. Once developed, leukemia is readily transmissible to other mice of the same inbred strain, and such a continuously transplanted neoplastic disease is referred to as a "line." Different lines of transplanted leukemia have distinctive characteristics. For example, one line, although failing to produce a local growth at the site of inoculation, is rapidly disseminated and the host mouse dies in about two weeks' time with generalized leukemia. Transplantation of another line results in a large local tumor growth at the site of transplantation, and the host mouse may live four to six weeks before malignant cells appear in the peripheral blood. The cells of other leukemia lines may preferentially infiltrate the ovaries or the kidneys, yet, despite the difference in biological behavior, no morphological difference between the cells has been detected. These observations emphasize the complexities of the leukemic cell and the uniqueness of each separate neoplasm. It has been noted repeatedly that when a line of leukemia is continuously transplanted, there is an increase in so-called "virulence." Thus a line, which in the first transplant generation produced leukemia in only a small percentage of mice of the same inbred strain, may, after a number of passages, produce the disease in 100 percent of the inoculated animals. The first generation transplant may have killed the host mouse after a period of several weeks, but, after continuous transplantation, the same line may kill in 10 days or less. Other types of transplanted tumors, hepatomas, and squamous cell carcinomas, for example, have behaved in a similar manner, and develop increasing virulence following repeated animal passage. It is possible that the increasing "malignancy" sometimes observed in human neoplasms, which is indicated by decreasing differentiation of the cells and increasing growth rate following metastasis or recurrence after excision, is a comparable phenomenon.

2. *Reticulum cell sarcoma.* In our experience, reticulum cell sarcoma is second to lymphocytic leukemia in frequency of incidence in mice. Incidence of neoplasms, however, is largely dependent upon the strains of mice commonly used, and other laboratories using different strains of mice report a greater incidence of granulocytic leukemia. Reticulum cell sarcoma may begin at any one of various sites in the body, but it nearly always eventually involves the liver, and this organ becomes enormously enlarged. Upon microscopic examination, the neoplasm consists of spindle cells and round or oval cells, and occasional multinucleated giant cells (figure 2). The mononuclear cells sometimes appear detached in the tissues or may be found within vessels. Malignant monocytes appear in the peripheral blood. These features suggest a neoplastic reproduction of reticuloendothelial cells. Some forms of reticulum cell sarcoma are said to resemble Hodgkin's disease in human beings. As a rule when reticulum cell sarcoma is transplanted subcutaneously in a mouse its behavior resembles very closely that of the primary tumor; usually no local growth arises at the site of injection, but the liver enlarges after a prolonged period of nine months or more and the mouse dies.

Bilirubin crystals have been found in these tumors. The presence of these crystals may reflect a functional activity of the tumor cells, since the site of bile pigment formation in the normal animal is now considered to be the reticuloendothelial system.

3. *Granulocytic leukemia.* Although granulocytic leukemia constitutes the most frequent form of leukemia in man, it is rarely found in mice. Even when present its incidence is much lower than that of lymphocytic leukemia in the same inbred strains of mice. Since the lymphocyte is the preponderant leukocyte in the peripheral blood of the normal mouse, it is possible that the relative abundance of this cell type may be responsible in part for the high incidence of lymphocytic leukemia.

Granulocytes, on the other hand, are normally about 20 percent of the leucocytes. In granulocytic leukemia in the mouse the spleen is generally enlarged, whereas the lymph nodes may be little affected. Relatively undifferentiated cells of the granulocytic series may be found in large numbers in the peripheral blood, and similar cells will be found infiltrating the tissues (figure 3). Granulocytic leukemia accompanied by the green discoloration of chlorosis has been described in rats, but this feature of the disease is rare in mice.

One difficulty in diagnosing granulocytic leukemia in the mouse is the facility with which mice develop an extreme leukemoid reaction and myeloid metaplasia. The leucocytes of the peripheral blood may reach nearly a million, yet these are non-neoplastic cells which will not grow on transplantation. Although the predominant cell is a mature granulocyte, immature forms are found as well, and great enlargement of the spleen and liver develops as a result of extramedullary hematopoiesis (figure 4). Some experimental work in leukemia is of doubtful value because this leukemoid reaction was not recognized. The leukemoid reaction develops after certain infections in mice, but the most extreme increase in granulocytes which we have seen accompanied the growth of particular tumors. When a true granulocytic leukemia is present, foci of cells of the

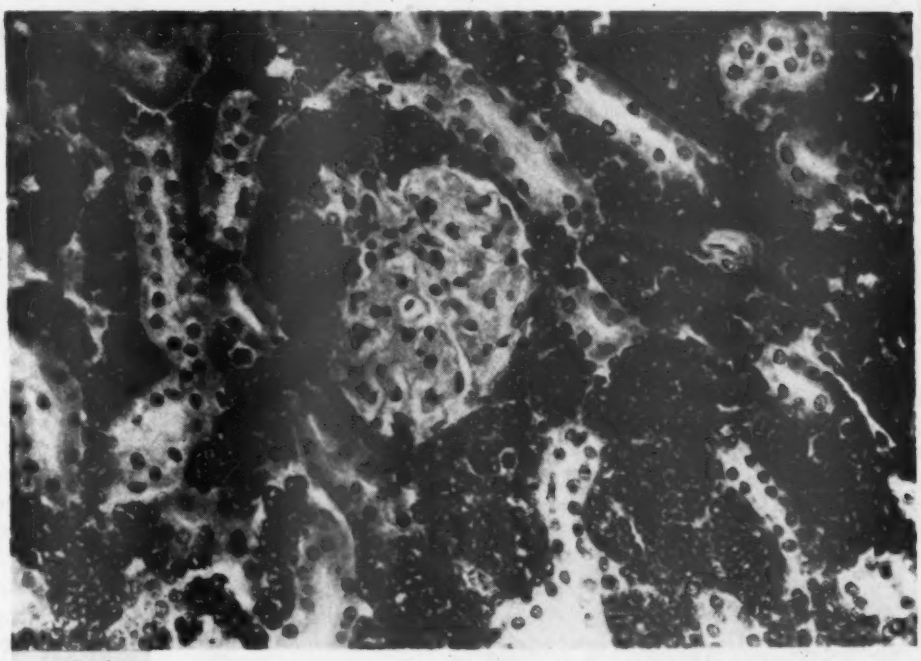

FIG. 1

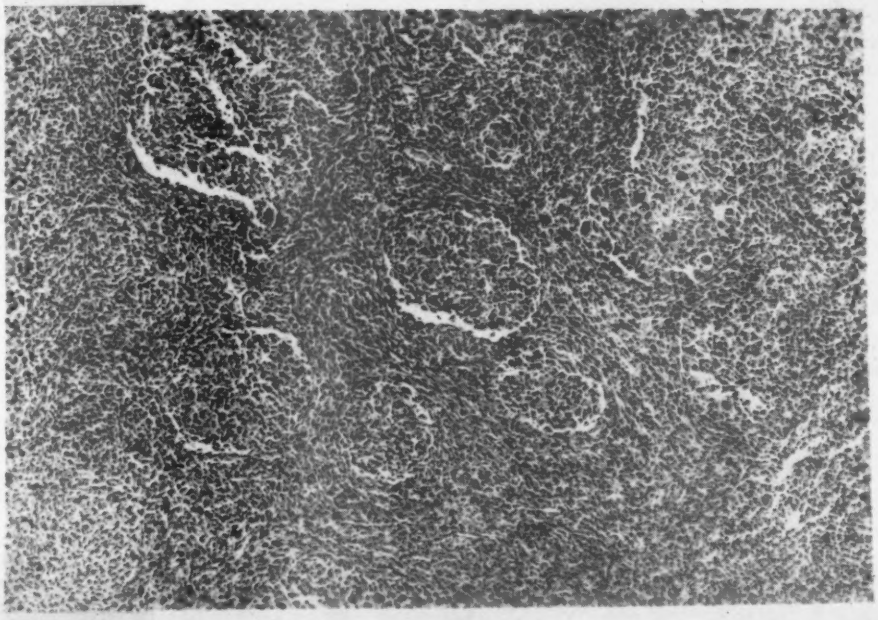

FIG. 2

Fig. 1. Lymphocytic leukemia infiltrating the kidney. Several mitotic figures can be seen. Hematoxylin and eosin. X800.

Fig. 2. Reticulum cell sarcoma. Observe spindle cells surrounding nests of round and oval cells. Multimuc'eate tumor giant cells are also present. Hematoxylin and eosin. X110.

granulocytic series can be found at sites in which myeloid metaplasia is not known to occur.

4. *Plasma cell leukemia.* This has recently been described in one strain of mouse from the Fibiger Laboratory in Denmark. Localized plasmocytomas were present, and neoplastic plasma cells were found within blood vessels. It was remarked in the discussion of these cases that all types of leukemia described in man had now been found in the mouse. We have seen one case diagnosed as a plasmacytoma in a mouse (figure 5).

5. *Mast cell leukemia.* No unquestioned case of this form of leukemia has been reported in man, although a great increase in blood basophils may be associated with myelogenous leukemia in man. In the mouse, tissue mast cells have often been reported closely associated with different types of neoplasm, particularly fibrosarcomas. After transplantation of the tumor, the mast cells can still be found and they apparently proliferate along with the growing tumor. They are also found in great abundance in the subcutaneous tissues after the skin surface has been painted with tar or other carcinogenic agents. This finding of mast cells in association with other neoplastic diseases in both man and mouse has stimulated experimental work and speculation as to the role of this cell in relation to cancer.

Aside from this secondary association of mast cells with cancer, a few cases of what appears to be a primary mast cell leukemia have been found in the mouse. Widespread infiltration of mast cells was found in many organs. Localized masses of abnormal mast cells, or mastocytomas, have also been described (figure 6).

Research on Leukemia in Mice

Those engaged in cancer research are convinced that leukemia in the mouse is a neoplastic process and that it is closely analogous to neoplastic diseases of the blood and blood-forming organs in man. Because of its similarity to human leukemia, its availability in high and low leukemic strains of mice, and the easy transmission of most lines, lymphocytic leukemia in mice has been utilized in many types of research.

1. *Morphology and biologic behavior.* Leukemic cells are readily separated, so that individual cells can be studied in smears under direct light microscopy and by phase and electron microscopy. No absolute single criterion has been found by which the normal and leukemic blood cells can be differentiated. The hypothesis that the leukemic cell is simply an immature or undifferentiated cell merely lacking the stimulus for maturation is not supported by research on animals.

A pre-neoplastic lesion, consisting of a localized reticulum cell hyperplasia in the lymph nodes has been described in high leukemic strains of mice. Similar lesions, however, have been observed in old mice from other strains, so that pathologists are not satisfied that a pre-leukemic lesion has been correctly identified. Recognition of the alterations which precede the development of unquestionable cancer is a notable advance in several forms of neoplasia, and it is to be hoped that this will some day be realized for leukemia.

Some pathologists who have studied large numbers of cases of human leukemia are of the opinion that there is a close interrelationship between different forms of malignant lymphoma and lymphatic and monocytic leukemia. These different forms of neoplasm are considered to be various histologic expressions of a single disease. Observations in mice somewhat support this point of view, for the strains which develop lymphocytic leukemia are generally the same strains in which the rarer forms of leukemia are also found.

2. *Genetics.* A long series of experiments has been carried out in one laboratory in which one high leukemic strain and one low leukemic strain of mouse were developed. Various crosses between these strains indicate that the inheritance of susceptibility to leukemia depends upon the percent heredity from the high leukemic stock. The influence of the low leukemic strain may mask or inhibit the leukemia-producing tendencies derived from the high leukemic strain. Similar experiments have been repeated in other laboratories with comparable results. Many genetic factors are involved in the development of spontaneous leukemia, and many modifying extrinsic factors have been revealed. An evaluation of the factors inducing leukemia becomes exceedingly complex. In general, leukemia can be elicited only in mice of those strains in which a natural susceptibility exists, and extrinsic factors often seem merely to hasten the appearance of the disease that otherwise would have developed inevitably at a later age.

3. *Extrinsic factors.* Among the known extrinsic factors, or leukemogens, are irradiation and exposure to chemical carcinogenic agents. Both of these factors usually produce an initial injury and subsequent atrophy of the hematopoietic tissues. Leukemogenic factors may not be equally powerful in their effects on mice of different strains. A strain resistant to the action of x-ray may be susceptible to the effect of 20-methylcholanthrene, and vice versa.

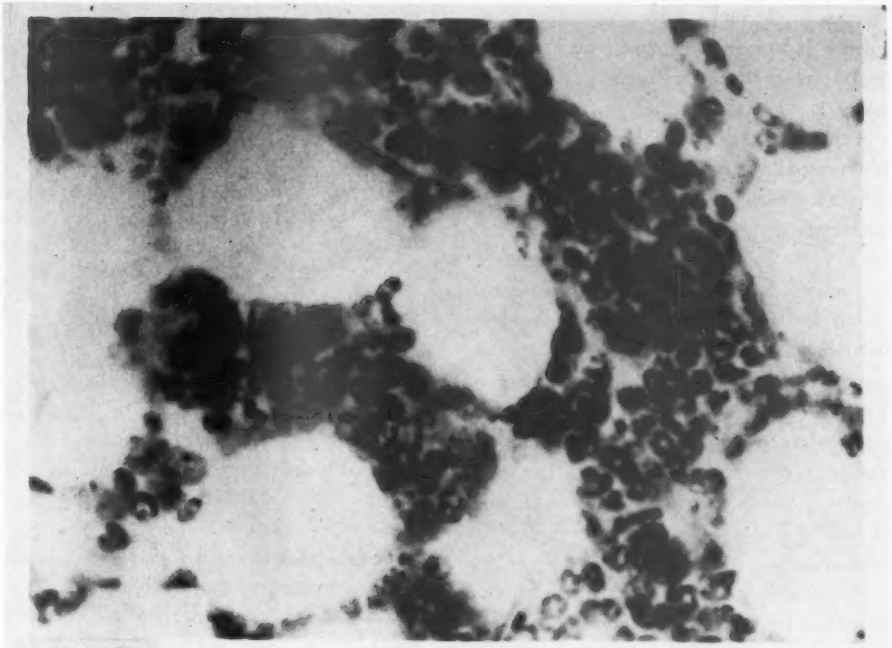

FIG. 3

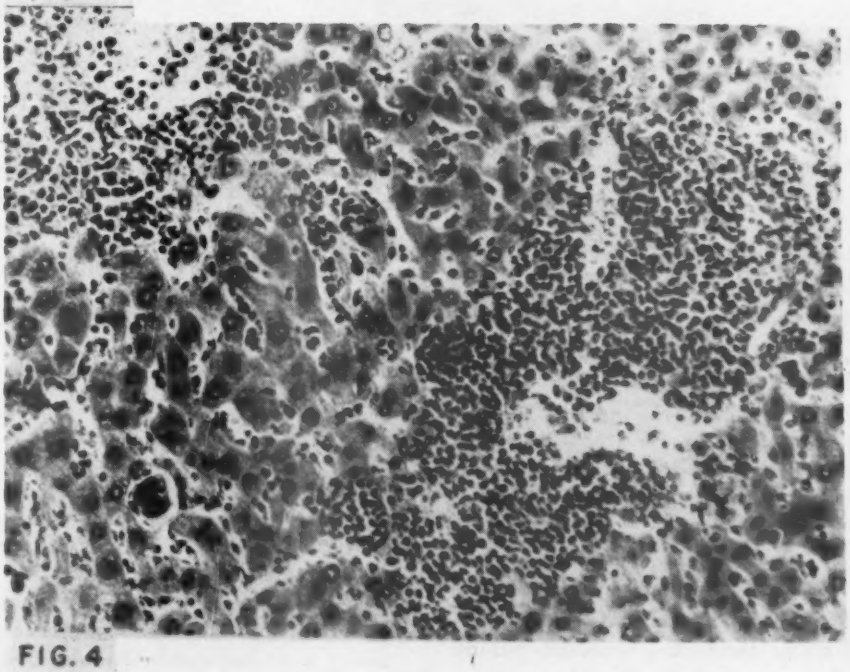

FIG. 4

Fig. 3. Granulocytic leukemia infiltrating adipose tissue. Observe large mononuclear myelocytic cells, and smaller cells with "doughnut" nuclei, characteristic of the mature granulocyte in the mouse. Giemsa stain. X880.

Fig. 4. Liver showing extramedullary hematopoiesis. Many granulocytic cells are present, and one large megakaryocyte. This condition is sometimes confused with leukemia. Hematoxylin and eosin. X280.

Other factors producing a detectable influence on the incidence of leukemia are female sex hormones and dietary modification. Unlike leukemia of human beings, the incidence of leukemia in mice is greater in the female than in the male; and estrogens are reported to have a leukemogenic action in mice of certain strains. The female mouse, however, has a longer life span than the male, and, since the incidence of leukemia increases with age, this factor must be considered in estimating a sex difference. Severe caloric restriction at an early age sufficient to depress development of lymphoid tissue reduces the incidence of leukemia, but has little effect on the disease once established. Cortisone has caused a temporary regression in some lines of leukemia, an effect that seems to be compatible with the fact that this hormone depresses lymphocytes in normal animals. It has been observed that a more advanced parturition age of the mother results in a lower incidence of leukemia in the offspring. No satisfactory explanation for this has been found.

4. *Chemotherapy.* Mice with leukemia have been used for testing chemotherapeutic agents. It is reassuring to find that the same substances which are proving effective against mouse leukemia are also effective in treating leukemia in man. In leukemia in man the effect of a drug in a particular case is not always predictable, and its usefulness must be determined by trial. A similar variation in response to different agents is found in mice with leukemia. Certain lines of leukemia have responded dramatically to aminopterin at an optimum dose level, while other lines have been relatively resistant. X-ray, urethane, nitrogen mustard, arsenic, and cortisone will influence the course of leukemia in mice, and life may often be considerably prolonged. As in human leukemia, however, no real cures have been effected. Since certain lines of leukemia are well standardized and kill all inoculated mice in a short period of time, they may serve as reliable test objects. It seems highly improbable that any effective agent will be found for mouse leukemia which will not be effective under suitable conditions for leukemia in man. One disconcerting observation recently made is that certain leukemia lines in mice apparently become resistant to certain agents (and may even grow more vigorously in the presence of the agent), just as sulfonamide resistance develops in bacteria. If a similar resistance develops in human leukemia, this may explain some of the failures after initial success with chemotherapy.

5. *Current research.* Current research on leukemia in mice follows diverse directions. It was observed that lymphocytic leukemia in certain strains of mice often began in the thymus, and that removal of the thymus at an early age significantly reduced the incidence of leukemia. Such an effect was to be expected since it eliminated the most susceptible organ. Recent experiments on a strain of mice in which the leukemia usually originated from tissues other than the thymus reveal a significant reduction in leukemia following thymectomy at an early age. This raises the question as to whether the thymus may not have a more important role in the origin of leukemia than can be explained by its high content of lymphocytes or its susceptibility to leukemia.

The presence of contaminant viruses in leukemic lines and their effect on the behavior of the leukemic process have recently been reported. These contaminants have modified the response of the host, and occasionally the contaminant has retarded the development of leukemia and prolonged life. These observations stress the possible existence of other complications in leukemia research, namely modifying viruses. This gives experimental support to recent reports that viral diseases, such as chickenpox in children, may modify the usual clinical course of leukemia.

The importance of the participation of virologists in research on lekuemia has long been recognized, and the theory that a virus may be the cause of mammalian leukemia has not yet been abandoned. The existence of a factor such as the milk agent of mammary tumors has not been found in leukemia after repeated trials of foster nursing.

A recent report that requires confirmation describes the successful transmission of leukemia to newborn mice of a different inbred strain. Adults of the same strain were resistant. It was further reported that when extracts of embryos from a high leukemic strain were injected into newborn mice of a low leukemic strain, the incidence of leukemia was significantly increased when the injected mice reached a leukemia-producing age. Should this prove to be true, it would be difficult to avoid the conclusion that leukemia may be initiated in the adult by an agent (or "virus") acquired in the first few days of life, but long dormant.

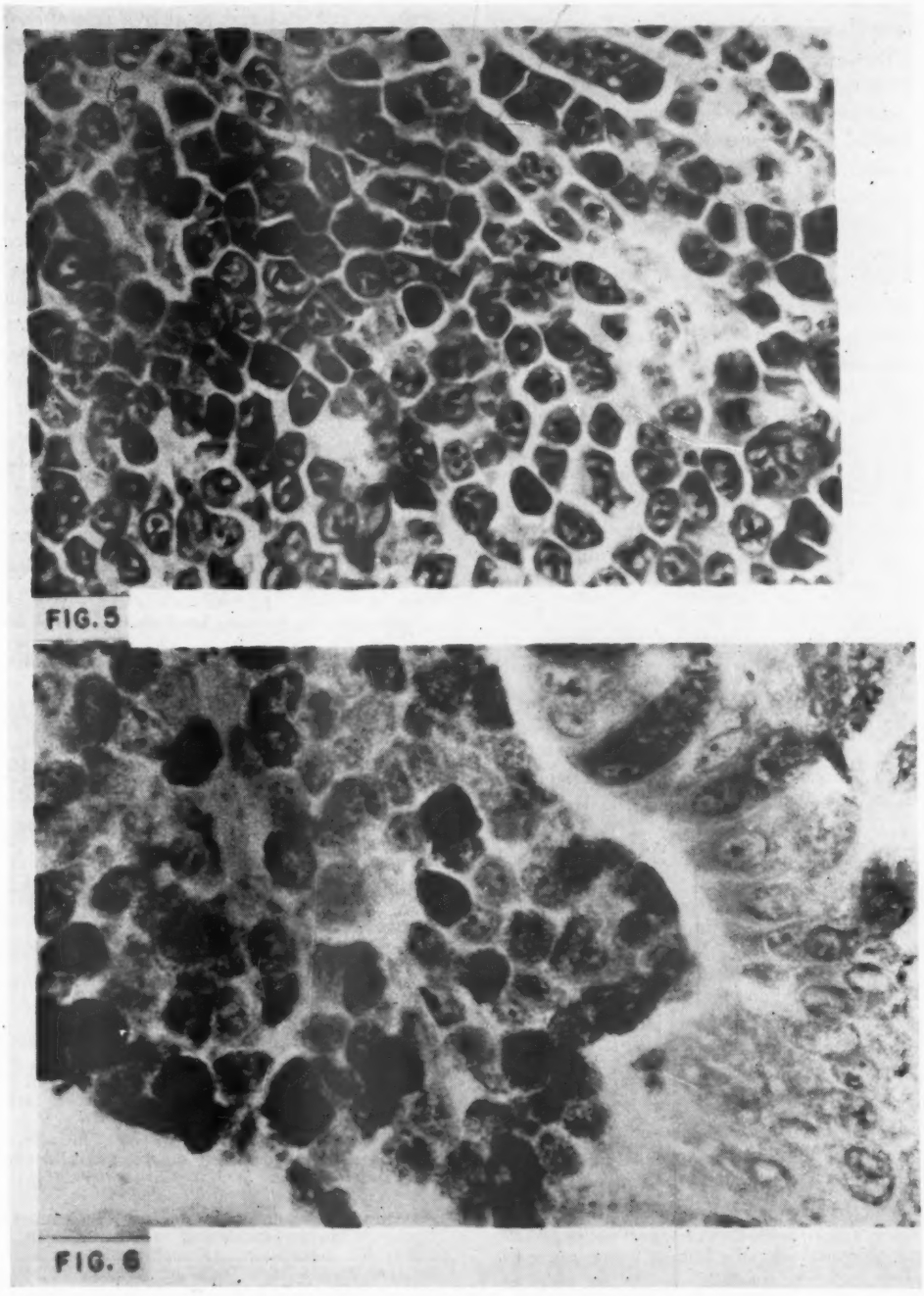

Fig. 5. Plasmacytoma. Localized collection of neoplastic plasma cells. Giemsa stain. X690.

Fig. 6. Mast cell neoplasm, showing large cells with granules stained by toluidine blue. X1000.

Conclusion

While the work on leukemia in mice may be of great theoretical interest, and potentially of real practical value, the clinician desires information that may be immediately helpful to the patient or his family. Great caution must be practiced in transposing the facts established about diseases in animals to similar diseases in man. Nevertheless, it seems safe to make certain assumptions regarding heredity, external stimuli, clinical course, and therapy of leukemia in man, basing these assumptions on well established facts regarding the disease in mice.

Heredity. Establishment of facts concerning hereditary susceptibility in the mouse has required years of inbreeding by brother-sister mating, a condition which does not exist in human families. When a case of leukemia develops in man, other members of the family may be assured that there is little likelihood of additional cases in the family. Although the hereditary factor may exist in leukemia (as in other diseases) it is so dilute in the human family as not to be of practical significance.

External stimuli. Leukemia can be induced in susceptible mice at an earlier age than it usually appears, by the action of certain external stimuli. Among these inducing factors are irradiation and chemical carcinogens. Inflammatory reactions and bacterial infections have not been shown to induce leukemia in mice, and it has not been established that such factors cause leukemia in human beings, although human leukemia is often first observed following acute infections. There is no evidence that leukemia in the mouse is infectious. A very drastic reduction in caloric intake has been shown to result in a lower incidence of leukemia in mice, but such severe dietary regimen also interferes with normal development and reproduction. Other modifications in diet have had little effect on leukemia in mice, and diet does not appear to be a factor in man. Some reports of experiments in mice indicate that benzene is leukemogenic, and exposure to this toxic agent may have initiated some cases of human leukemia. Exposure to x-ray appears to increase the incidence of leukemia in both man and mouse. Physicians and technicians should be protected in every possible way from such exposure. In the ordinary course of life, the human being is not exposed to known or avoidable conditions which increase the liability of leukemia.

Clinical course. Spontaneous leukemia is as inevitably fatal in mice as it is in man. There is, however, considerable variation in the behavior of different spontaneous and transplantable lines of leukemia and the length of survival time of the host animal. Similarly, leukemia in human beings shows differences in the rate of progression.

Therapy. Research on leukemia in mice proves conclusively that certain agents can significantly retard the progress of the disease. This effect has been measured in carefully matched groups of control and experimental mice, inoculated with the same dose of leukemic cells. No such standardization of human leukemia is possible, and there is so much variability in the course of the disease that considerable clinical judgment and experience are required to estimate the effects of therapy. The undoubted prolongation of life in mice is reason for encouragement and hope that a truly effective cure for leukemia in man may some day be achieved. In the meantime, an active program of research should continue the progress that has been made in the past decade.

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Effect of Conscious Anxiety on the Electrocardiogram

Ruth B. Benedict, M.D.

A CONSIDERABLE NUMBER of publications dealing with electrocardiographic changes in neurocirculatory asthenia[1,2] and in psychotics and severe neurotics[2,4,5,6] have appeared in the literature of the past two decades, but little work has been reported on the effects of a specific emotional stimulus on the electrocardiogram. The most frequently quoted papers on this subject are those of Mainzer and Krause[7,8] who reported on the effects of fear on the electrocardiogram. Since their work is limited to the standard limb leads and since their conclusions seem rather far-reaching, it was thought worth while to reinvestigate this subject.

METHODS

Fifty medical students about to take a major examination were the subjects of this study for which all had volunteered. Forty-seven students were in their twenties and three were in their thirties. Forty-four were men and six were women. Each student had a heart and blood pressure examination. A few cardiac fluoroscopies were done when indicated. Control electrocardiograms using limb leads, six precordial V leads, and Goldberger extremity leads were done on all subjects. A double Master exercise tolerance test completed the preliminary study. Each student was again seen about one hour before the examination. None had smoked in the preceding hour. Each was questioned briefly about the state of his feelings, the presence of physical symptoms accompanying tension, the amount of sleep he had had the preceding night, and the ingestion of stimulants. Physical signs such as flushing, sweating, tremor, and so on were looked for. The 12 lead electrocardiogram and exercise tolerance test were then repeated.

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OBSERVATIONS

All but two students had normal cardiovascular findings. One had inactive rheumatic heart disease with mitral insufficiency, a slightly enlarged heart, and good compensation. Another had a blood pressure which ranged from 150 to 190 systolic and from 90 to 100 diastolic. Forty-eight students stated in their preliminary interviews that they considered examinations a definite strain. Some individuals thought them a severe ordeal, while others classified them as a minor stress. Ten of the 50 students were particularly concerned about the impending examination: five because they were in danger of failing and five because of their desire to do especially well.

Several variations from the rigid standards of normal were found in the control electrocardiograms. One student had a PR interval of 0.24 seconds. A similar finding had been noted in a tracing done on him two years earlier. Another had a QRS duration of 0.11 seconds and had also been told of this two years previously. A third showed a T wave in lead one which was less than 1 mm. in height. These three men had no other evidence of cardiac abnormalities. Since all of these electrocardiographic variations have been found to occur in normal subjects,[9] it may be assumed that they were normal variants in these students as well. Ventricular premature contractions occurred in two students and auricular premature contractions were found in a third.

Interpretation of the exercise tolerance test was possible in 43 instances. In three records the string wandered so badly that readings were impossible. In the remaining four the test was incomplete. ST depressions were referred to the PQ level if this was lower than the beginning of P. Seven records were positive as judged by Master's criteria.[10] Each showed an ST depression of 0.5 mm. or more in at least one lead. No significant T wave changes were

seen. Another record was questionably positive as judged by these criteria. None of the control records were positive when judged by the criteria of Grossman, Weinstein, and Katz.[11]

On the day of the examination 41 students stated that they felt anxious. Thirty-one indicated that the stress was mild to moderate, while 10 felt they were undergoing a severe strain. Nine claimed to be unworried. Twenty-six students exhibited both signs and symptoms of nervous tension, 10 had signs only, 8 had symptoms only, and 6 showed neither. The commonest symptoms were urinary frequency, 13 (three of whom had had more coffee than usual); sweaty palms, or more generalized sweating, 12; poor appetite, 9; increase in number of bowel movements, 8; and dry mouth, 8. The most frequent signs were flush, 18; tremor, 13; marked sighing respiration, 7; and jerky speech, 6. Fourteen students said the exercise test seemed more strenuous than it had on the day of the control.

When the heart rates of the control tracings were compared with those of the pre-examination records, it was found that there was an acceleration of 20 beats or more in 10 records and of 10 or more in another 20 records. Only 2 students had a somewhat slower rate on the day of the examination. In 21 students the heart rate after exercise was greater by 10 or more on the day of the examination. Premature contractions showed up in those students who had exhibited them previously and were about the same in number.

Of the three students with original PR intervals (each rechecked on at least two other occasions) of 0.20, 0.21, and 0.24 seconds, one showed a decrease of 0.04 seconds in this measurement and 2 of 0.05 seconds. None of these decreased PR intervals were associated with rate increases over 20. Three other students had control PR intervals of 0.20 seconds, but these showed no change in this measurement. Subjects with somewhat shorter PR intervals either showed no change in them or had a decrease of 0.01 seconds, 11; or of 0.02 seconds, 2.

P wave changes were insignificant.

No changes in QRS measurements occurred. There were some minor and unimportant changes in QRS configurations.

ST displacements were noted in eight tracings but were so minor and so obviously related to rate increases that no significance could be attributed to them.

Some T wave lowerings occurred in 23 records. In 19 of these the rate had increased by 10 or more, while in the others it showed practically no change. In one, also with an increased rate, the T waves throughout were somewhat higher. These changes, too, were thought to be within the normal range.

Only one student developed T wave changes which appeared worthy of note. This 27-year-old man felt moderately tense on the examination morning, but was unaware of any unusual physical symptoms. He had slept several hours less than usual on the previous night. While his control heart rate had been 80, it was 105 on the morning of the examination. His blood pressure had not changed appreciably. His tracings showed a change of T^1 from 2.5 to 1 mm., of T^2 from 2 mm. to an iseolectric notched configuration, of T^{AVL} from 1.5 mm. to 0.5 mm., and of T^{AVF} from 0.5 mm. upright to 0.5 mm. inverted. All precordial T waves were lowered. This was especially marked in V5 and V6 where previously upright waves had become flat. The changes in the limb leads resembled those described by Graybiel and White in the "startle reaction."[12]

In the exercise tolerance tests performed on the day of the examination, all tracings which previously had been positive according to Master's criteria were again found to be positive. One record which had previously been negative as judged by these standards became positive, but this was accompanied by an increase of 25 in the heart rate. Since the actual changes between the first and second records were not great, and since the heart rate had accelerated as much as it did, it appears unlikely that the positive test was the direct result of emotional stimuli. One student developed a positive exercise test according to the criteria suggested by Katz's group. Again the differences between the control and pre-examination tracings were not great, and again the heart rate had increased considerably.

Discussion

Since this study attempted to demonstrate electrocardiographic changes which might be induced by conscious anxiety, it is pertinent to inquire whether the situation used was a suitable one. From the subjective reports given by the students and from the objective observations made on them, it can be said that 20 percent were extremely apprehensive, while another 60 percent were moderately to mildly so. Though 20 percent claimed to be unworried and relaxed, observation showed that all of them were not. Other workers have used the pre-examination situation to study the effects of nervous strain on different physiologic functions, and their results confirm the observation that it is a situation of genuine stress. Thus, Dodge demonstrated that pulse rates taken after a stipulated rest period were higher on the morning of an examination than on other mornings.[13] Hickham, Cargill, and Golden

demonstrated an increase in the cardiac output of most medical students before a major examination. They also showed an increased pulse rate and a decreased peripheral resistance in many of their subjects.[14] Cannon mentions the appearance of sugar in the urine of 18 percent of nondiabetic students directly after an examination.[15] While these studies support the conclusion that examinations are a true source of nervous tension, it is also clear from the present investigation that the intensity of the strain varies considerably from subject to subject.

Significant electrocardiographic changes demonstrated here were few, despite the many other signs and symptoms of tension which these students exhibited. These findings are strikingly different from those of Mainzer and Krause who reported significant abnormal changes in two-fifths of 53 patients, 41 of whom had previously had normal tracings.[8] These workers used the preoperative situation as their fear producing stimulus. Since they were able to obtain records at the height of their patients' reactions (i.e., just as the anesthesia mask was being applied on the operating table), this situation probably represented a greater source of stress for some subjects than the one used in the present study. Forty of their subjects were females and this might conceivably have had some bearing on their results, though no changes were demonstrated in the six women who participated in the present study, despite the fact that a number of them were extremely apprehensive. While Mainzer and Krause stated they were studying the effects of fear, they did not interview their patients and so could not judge what degree of fear, if any, was experienced by them. These authors failed to define their criteria for ST and T wave changes, so that the significance of some of the changes which they interpreted as positive is doubtful. Since a number of their patients developed a considerable tachycardia, the high percentage of aberrations in this subgroup was probably a direct result of the increased heart rate. In addition, they included patients with pre-existing coronary heart disease in their study and made the unwarranted assumption that electrocardiographic changes in such patients were of the same nature as those in individuals with normal hearts.

Mainzer and Krause believe that the ST and T wave changes which they demonstrated were due to a decreased coronary blood flow resulting from local vasoconstriction induced by fear and mediated through the autonomic nervous system. While an inadequate coronary flow may actually have occurred in patients who already had disease of these arteries, a similar assumption cannot be made in healthy persons. The ST and T wave segments are the most labile portion of the electrocardiogram. Changes in them are nonspecific for anoxemia and may be induced by many different factors, such as tachycardia, the auricular T wave, heart position, chemical disturbances of the organism, and so on. Autonomic imbalance also appears to be a cause of ST and T wave alterations, but there is no proof that it induces its effect through coronary vasoconstruction or through myocardial ischemia produced in some other fashion. Conceivably autonomic factors may alter repolarisation of the cardiac muscle directly or may affect conduction within the heart and thus cause electrocardiographic changes. In the present study significant lowering of T waves, especially in leads 2, V5, and V6, was found in one student. When the ventricular gradient was figured for this tracing, the T wave change was found to be secondary and was, therefore, probably not due to an alteration in myocardial repolarisation.

The three students with labile PR intervals all had original measurements of 0.20 seconds, or over. The cardiac rate increases which they developed were not enough to account for the shortenings found. Katz[16] states that this measurement should be constant to within 0.04 seconds, so that in only two of the present cases can the change be called definitely abnormal. However, prolonged and variable PR intervals have been described previously in patients with neurocirculatory asthenia and in psychotics, so that it seems likely that emotional factors can effect this measurement. All three students who showed this shortening were tense on the day of the examination, and two were particularly concerned about the grade they would make. It, therefore, seems likely that these shortened PR intervals were the result of anxiety. Such a change in the PR interval may be mediated through the autonomic nervous system in view of the known action of the vagus nerve on this measurement.

The seven positive double Master exercise tolerance tests indicate that Master's criteria for the diagnosis of coronary disease are too lenient when applied to the double test. Biork, [17] Katz's group,[11] and others believe that this is also the case when these criteria are applied to the single test. These men feel that new standards need to be established, but so far there is no agreement as to what they should be. Those suggested by Grossman, Weinstein, and Katz would appear to be more reliable. Although Master has described exercise tolerance changes similar to those found in coronary heart disease in patients with neurocirculatory asthenia and in neurotic individuals,[10,18] no changes which

could definitely be ascribed to nervous tension were found in this study.

Other workers have studied the effects of emotion on the electrocardiogram by analyzing tracings of groups of patients with neurocirculatory asthenia, neurosis, and psychosis. While the present study approached the subject from a different angle, the small number of positive results obtained parallels the findings of such investigators as White and associates,[2] Friedman,[19] and so on, who found few and noncharacteristic changes in the conditions they studied. Though contrary opinions, based on rather similar data, have been expressed by Ruskin and coworkers,[5] Meyer and Billman,[4] and others, their reports reveal that they, like Mainzer and Krause, have tended to attach unwarranted significance to minor changes and have assumed that all aberrations encountered in their tracings were emotionally induced, whereas some were probably caused by other factors. Actually, it is probably fair to state that emotions can cause changes in the electrocardiogram of normal individuals, that this is a rather infrequent occurrence, and that its appearance will depend on the strength of the stimulus and the susceptibility of the individual.

Summary and Conclusions

The effect of conscious anxiety on the electrocardiogram was studied by taking control and pre-examination tracings on 50 medical students who had previously been examined and interviewed as described and who were observed on the day of the examination for evidences of nervous tension.

Eighty percent of the students were mildly to moderately anxious, and at least 20 percent were very apprehensive. Many exhibited physical signs and symptoms associated with anxiety.

Three students, all with control PR intervals of 0.20 seconds or over, showed a decrease of 0.04 seconds or more in this measurement.

Possibly significant T wave lowerings were found in one pre-examination record.

No significant changes which could definitely be ascribed to emotional stimulae were found in the double Master exercise tolerance test.

Conscious anxiety of the intensity described produces few electrocardiographic changes in healthy young subjects when the tracing is taken 30 to 60 minutes before the significant event.

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Home Care Service

GEORGE WASHINGTON UNIVERSITY CANCER CLINIC

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DIAGNOSIS: Carcinoma, incurable. With that written on a patient's case history, excellently trained physicians only too frequently lose interest and perfunctorily write prescriptions for narcotics until it is time to sign the death certificate. This may sound like harsh criticism of the profession. It is not intended as any reflection on professional ability, but rather as a reflection on the inability, in this day of specialization, of far too many doctors to consider their patients as human beings—to realize that someone on whom the diagnosis of carcinoma has been made is the same person after as before, but with the added emotional problems, both personal and interfamilial, which accompany the diagnosis of cancer.

It was with the purpose of making cancer patients more comfortable that the trustees of the Stewart Estate gave funds to the George Washington University Cancer Clinic (Warwick Memorial) to set up and run the Home Care Program, which started operating in February, 1950.

The Warwick Home Care Program is patterned, to a large extent, after the program of Montefiore Hospital, New York, where the idea for such a service in the home originated. However, the Montefiore program is set up to handle all kinds of diseases, whereas that of Warwick deals with cancer only. The Warwick program is designed to provide, for cancer patients who are unable to attend clinic routinely, medical, social work, and other hospital services which, on the whole, would not be accessible to such patients either for financial reasons or for lack of available institutional care, or because of the patient's adverseness to institutionalization.

As a matter of fact, the very nature of the disease, its chronicity, with not a straight downhill course but rather a tendency to remissions and relapses, makes the home a much more suitable setting than a hospital ward for the patient. However, two factors are absolutely mandatory to success of the Home Care Program, namely, desire on the part of the family to keep the patient in the home and an adequate physical home set-up. There have been numerous persons referred to the Home Care Program who have not been acceptable because of the absence of one or the other above mentioned factors. These patients are not just turned away, but are carried on an emergency basis until some adequate disposition of their cases can be made. There were 43 such cases from July 1, 1950, to June 30, 1951.

The program is staffed by a medical director, a visiting physician, and a social worker, and is integrated with the Cancer Clinic facilities, so that auxiliary nursing, orderly, and medical services are available.

The medical director carries the overall responsibility for the program, handles administrative details, approves standards of medical procedure, reviews all cases once a week, and is responsible for taking one or two medical students once a week to the home of some patient presenting an interesting diagnostic or treatment problem. This is part of the senior student's training while on the out-patient service.

The visiting physician sees the patients at regular intervals, usually once a week, frequently more than once a week, occasionally bi-monthly, all depending upon the needs of the patient. On each visit the patient is examined to determine the progress or regression of the disease or to check on any other condition, such as hypertension or diabetes. When indicated, blood is secured for laboratory analysis, sternal punctures are made, thoracenteses or paracenteses are done, or tracheotomy and Levine tubes changed. If a consultant is needed or hospitalization is indicated, either for treatment or diagnosis, the visiting physician arranges for this. Detailed medical records such as those found in a teaching hospital are kept. The physician presents for discussion at the weekly Tumor Board Conference, those cases in which there is a problem, either in regard to diagnosis or to treatment.

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The social worker is a very important part of the program, acting as liaison agent between the doctor and patient and between the patient and community resources. It is her job to evaluate prospective patients as to whether, from the home standpoint, they can or cannot be accepted under the Home Care Program. She makes arrangements for visiting nurses or housekeepers to go into the home when needed, which arrangements are frequently essential for making it possible to maintain the patient at home. The social worker helps the family to secure dressings from the American Cancer Society, to solve the financial problem involved in hospitalization when such is indicated, and to arrange emergency transportation to the hospital or clinic by the Red Cross when the home care station wagon is in use. But most important of all, the social worker, being a lay person, acts as a sounding board. Frequently, patients fail to understand the importance of medical orders and, hesitant to speak to the doctor, turn to the social worker for further explanation. In such instances she has a golden opportunity to integrate more closely the medical program with the patient and family. This is particularly important in research cases where new medicines or procedures are being used. Moreover, as the patient and family recognize the social worker as a lay person, they feel free to discuss their emotional and financial problems with her, and she not only helps in the resolution of these problems but, in turn, brings the attention of the physician to those aspects which are of medical significance. She is also very helpful at times in making it possible to secure permission for autopsies. To sum up the function of the social worker, one may say that she is the pivot around which the program revolves.

While this staff organization may appear novel in certain respects, actually the Home Care Program attempts to care for the patient at home just as though he were in the hospital. As a matter of fact, all emergency night calls are handled by two hospital residents. Being associated with a teaching hospital and medical school, the Home Care Program has available laboratory and x-ray facilities, consultants in all specialized fields, a weekly Tumor Board Conference, and facilities for giving transfusions and evaluating new experimental drugs.

There are financial resources from the grant for the Home Care Program for supplying medications to those patients unable to afford them. Narcotics alone, in the quantities used by cancer patients, can upset even an average family's budget, and antibiotics and other special medications (cancer patients may also contract pneumonia, urinary tract infections, and other complications) can completely undermine it.

It has been possible to secure surplus foodstuffs such as powdered milk and eggs. The baby food companies have contributed cases of pureed foods which cannot be sold because of slight discoloration but which are perfectly safe from a health standpoint. Procuring these foodstuffs has enabled many tube-fed patients to have a more adequate diet than otherwise would have been possible.

Who may be a patient under the program? Provided there is an adequate home set-up and that home care is desired, anyone with cancer who has become physically unable to make routine visits to the clinic may qualify, regardless of race or financial status. Most patients have been of the lower middle class, although there have been some in the upper income bracket as well as total indigents. Those patients with adequate incomes usually retain their own physician, under whose direction the home care physician works. There is a moderate fee for home care service in such cases.

Patients have been referred to the program by cancer clinics, social agencies, hospitals, private physicians who find it no longer feasible to carry the patient alone, the cancer research division of the National Institute of Health, and by self-referral after articles concerning the program have appeared in the newspapers. The case load varies from 10 to 25 patients, averaging about 18.

From July 1, 1950, to June 30, 1951, 67 new patients were admitted to the service, while an additional 19 were carried over from the previous five months. Of these 86 patients, 22 died at home, 38 in the hospital, and 13 were still carried as of July 1, 1951. Of the remaining 13 patients, 11 were transferred to the out-patient department, and 2 resumed private physicians' full care. The Home Care Service gave a total of 4,724 patient days of service. Visits by the physician to the home totaled 620 and to the hospital, 168.

Typical Case History

CASE 812-50 was a 46-year-old painter who in the early spring of 1950 started complaining of increasing loss of vision, severe headaches, and difficulty in using his arms and legs properly. A diagnosis of bronchogenic carcinoma with metastases to the cerebral hemispheres was made by a private physician who then referred the case to Warwick Clinic.

May 12, 1950, the left internal carotid artery was cannulized for the administration of nitrogen mustard of which a total of 20 mg. was given. Patient was discharged June 6, 1950, to the Home Care Service. Several visits were made by the Home Care physician, who noted a gradual improvement of vision and gait.

However, by early August there developed marked aphasia, loss of vision, very unsteady gait, and almost complete loss of the use of the right hand.

The patient's case was brought up before the Tumor Board Conference and it was decided to give him a second course of mustard. Between August 2 and August 12, 49 mg. were administered, and the patient was again discharged to the Home Care Service. Weekly visits were made by the doctor. At each visit a neurologic examination was done and the chest examined. The doctor arranged for the man to receive, as an out-patient, x-ray therapy to his skull. By September 26, the patient showed dramatic improvement, his gait was almost normal, there was almost perfect function of the right hand, light and the shape of large objects could be discerned, and there were no headaches. Since the patient could easily be brought to the clinic, he was discharged to the out-patient department and placed on emergency Home Care Service only.

On March 20, 1951, the patient was unable to keep his clinic appointment. A visit was made by the Home Care doctor who decided to accept the patient back on the Service. The patient went rapidly down hill. On each visit the neurologic examination revealed increasing brain involvement. The Home Care Service furnished a hospital bed and narcotics for the severe headaches. When the patient became incontinent, the American Cancer Society furnished pads. On May 12, the patient became unconscious and hospital arrangements were made by the Home Care physician, upon the wife's request. The patient died on May 18. An autopsy was performed, which confirmed the original diagnosis.

Having a cancer patient in the home is at best a strain for all concerned. At worst, it creates such tensions and worries that the stability of the family is threatened if not shattered. From the response of the patients and their families, it is known that the Home Care Program's major contribution lies in the sphere of maintaining morale—physical, mental, and financial. It is taken for granted that the patient, with very few exceptions, will die of his disease, and thus cure is not the objective as it usually is in medical practice. In other words, the program is not designed primarily to prolong life, but rather to make patients more comfortable to the end. It is designed to give cancer patients the mental security which comes from knowing that someone is still interested in their physical welfare; to give the families of such patients the security of knowing that they have people to turn to for help and reassurance. Frequently observed is a lessening of patient-family tensions, when the family feels that the patient is receiving interested medical attention and when the patient realizes that the family is being helped financially so that he or she is no longer a complete burden.

Since the program is planned, to a large extent, to work through the technique of psychologic reassurance, it may be well to review briefly a few of the problems the physician is apt to encounter along this line.

Probably the most frequently asked question by a cancer patient's family is "How long will he (or she) live?" And in fairness to the family, as well as to save the physician a great deal of later embarrassment, that question cannot be answered without much qualification. One of the most striking aspects of cancer is the fact that it is not a disease which runs a predictable, straight course; more often its course is long and circuitous, with many ups and downs. There are frequently dramatic spontaneous symptomatic improvements following almost terminal states. No one can explain why. More often than not the remission occurs regardless of, rather than because of, medical care. Imagine the reaction of a patient and his family, as it occurred in one instance before the patient came under the Home Care Program, if told that death would be a matter of days and actually it did not occur for some fourteen months. When working solely with cancer patients, a physician learns to concentrate medical effort on the daily welfare of the patient and look upon this service as the major contribution. By doing this, the physician will make the patient feel better as a human being and thus relax. As a consequence, concern over the duration of life becomes much less important.

Another question frequently asked by either the patient or the family is "Can one catch cancer?" It is hard to believe that, in this day and age, some intelligent, educated people are still under the delusion that cancer is as contagious as measles. Relatives of patients will spend harrassed hours boiling the dishes and clothes and bedding of the afflicted member of the family and living in real terror that through their necessary contact with the patient they, too, will contract the disease. The relief which comes from the knowledge that there is no real danger of "catching" cancer often makes the family *want* to keep the patient at home and, again, lessens patient-family relationship tensions. After all, when a patient is treated physically almost like a leper, he or she cannot help feeling rejected, no matter how much verbal front the family maintains.

Still another question asked, and one which poses a real problem for the physician is, "Should we tell him what he really has?" or, even more often, "Please, doctor, you won't tell Mary what's really the matter, will you?" For those patients diagnosed at Warwick Clinic this is no problem. Almost without exception they know their diagnosis and, frequently, the extent of their disease. Such patients, on the whole, have a very healthy and stable attitude towards, and acceptance of, the diagnosis. An illustrative case is that of a 79-year-old lady who used to discuss her impending demise with the noncha-

lance of a woman talking about a recent shopping expedition, and everyone involved felt perfectly at ease. Quite often one hears people say, "If I knew I had cancer I would kill myself." But they don't; in fact, they tend to cling to life with the utmost tenacity. In all the cases that the Home Care Program has handled in the past 15 months there has been one instance of suicide, occurring in the very initial stage of home care treatment.

From contact with those patients who supposedly do not know their diagnosis, it may be said that by far the great majority know perfectly well what is the matter. They do not come out and say so, either because they cannot emotionally accept the diagnosis or because they think their families do not want them to know. For those very few individuals who cannot emotionally accept a fatal diagnosis, there is no point in forcing the issue unless there is some specific reason which makes it necessary. It only upsets the person and changes him from a manageable patient to an almost unmanageable one. In most of those cases where it is believed that the patient knows the diagnosis but has not been told specifically, the family has been encouraged to be frank. They have been told not to emphasize the diagnosis, not to harp on it, but to have an understanding with the patient that this is just one more experience to share and to see through together, not to hide from one another. This approach has been found to have a great emotional therapeutic value to both patient and family, who then can let down their mental fences and relax together. There is so much truth to the old adage, "Ignorance breeds fear."

Occasionally there will be enough remission of symptoms to enable the patient to be taken off home care and made a clinic patient instead. At times there has been some difficulty in convincing a family that this is the wisest course of action to take, even if the remission is of short duration. Psychologically, it gives the patient's morale a boost to know that he or she is no longer housebound, or dependent on medical services being given in the home. The normal human being has a great urge to be independent. When this change from home to clinic status occurs, the patient and family are informed that the Home Care Program will be at their service in any emergency or whenever it becomes necessary.

It has greatly surprised a number of the medical profession who have come to know about the Home Care Program that only one of the program's patients has ever required morphine injections, and that one patient only during the last few days before his demise. It should also be noted that the patients are not lying in pain. By starting patients off on the mildest form of medication which will ease the pain—sometimes this being mere aspirin and/or one-fourth grain codeine tablets, the latter being gradually increased to a maximum before changing to demerol—it has been found almost totally unnecessary to use morphine. Another technique is to switch back and forth between codeine and demerol so that the tolerance to both drugs is slower to develop. Unfortunately, if a patient is started immediately on morphine (which only too often occurs), it is almost impossible to do anything else than give increasing doses of it. Although there is no medical objection to morphine, the use of any drug requiring hypodermic injection is not feasible for home care purposes, since it usually has to be administered by a member of the patient's family, and if a member of the family is not willing to administer the drug, hospitalization or some form of institutionalization becomes a necessity. Some families are hesitant to give narcotics in sufficient dosage to keep a patient comfortable. They are afraid the patient will become addicted. When it is explained that the patient will continue to need narcotics to keep from suffering, and that whether or not addiction occurs is relatively unimportant, because he will never get well, the reluctance is overcome. Keeping the patient comfortable should be the prime motive.

Another problem is whether or not hospitalization should be urged when death is imminent. If the family is willing to have the patient die at home and is fully aware of all that this may entail—such as a severe hemorrhage or unconsciousness with all the complications that ensue—there is rarely any reason to urge hospitalization. A large percentage of home care patients are kept at home until death. However, if the family seems to be reaching the end of its emotional and physical rope, hospitalization is advised, and as much help as possible is given to make the best financial arrangements. Sometimes it is necessary to explain to a patient who does not want to be removed from the home why it is wise to accept hospitalization. It is not right that a family be left completely drained physically and emotionally after a member's death.

When, as has happened almost without exception, the family of a recently deceased home care patient calls up the office and says, "We are so grateful for all you've done for us," or "We don't know how we could have got along without your service," the Home Care Program staff feels "Mission accomplished."

Current Concepts in Allergy

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IMMUNOLOGY, or allergy in its broadest sense, embraces such a variety of manifestations that a great deal of confusion results unless the subject is divided into major categories of antigen-antibody reaction. Most of the known manifestations of allergy or immunity can be classified as follows: immune reaction, red blood cell factors, anaphylaxis, bacterial sensitivity as characterized by the cutaneous tuberculin reaction, serum or drug sickness, contact-type dermatitis, and atopy. This article will describe the field of immunology with reference to this breakdown pattern and will review a few of the stimulating discoveries made in recent years.

Immune Reaction

Protective antibodies result from either clinical or subclinical infections, or they may be deliberately induced by artificial immunization. Immune antibodies are found in the gamma globulin component of blood serum and augment the resistance of a host to disease in such ways as clumping invading bacteria, facilitating their engulfment by phagocytes, and neutralizing toxins and viruses.

The distribution of antigen in experimental animals has been the subject of repeated investigations. the bulk of antigenic materials studied (tetanus toxin,[1] arsenic-labelled horse serum,[2] a particulate solution of a red azoprotein,[3] and radioactive viral and protein antigens[4]) have been found primarily in the reticuloendothelial system. Florence Sabin reported that fibroblasts also picked up some particles of antigenic dye and that polymorphonuclear cells picked up the antigen, apparently transporting it to reticuloendothelial cells. Kruse and McMaster[5] have reported that after administering a blue colored antigenic dye to mice either intracutaneously or intravenously, the antigen eventually was found in all organs except the brain. When the injection was made in the tail veins of mice, the heaviest concentrations of antigen were found in liver, mesenteric lymph nodes, and kidney tubules. The antigen was found to remain in the tissues as long as three and one-half months, although it could be detected in the blood only until the twelfth day. Smetana,[6] also using a dye-antigen, found ample antigen still present in the reticuloendothelial system 28 days after injection. Sabin reported decided diminution of her particulate dye-antigen by the seventh day. Kaplan and his co-workers[7] reported that pneumococcal polysaccharide antigen was still present at 75 days in macrophages, a few lymphocytes, kidney capillary endothelium, hepatic cells, Küpffer cells, and myocardial cells. It is not unreasonable to suppose that the retention of antigen in the tissues may vary with the individual antigen in question. Ehrich[8] and his co-workers have shown that bacillary antigen injected in a rabbit's hind foot pad travels within a few hours to the regional lymph nodes and subsequently through the efferent lymph to the general circulation. The regional nodes are the first to swell with actively proliferating lymphoid tissue. By the third or fourth day antibody production is evident and the node is overrun by lymphocytes and plasma cells, one or both of which produce specific antibody protein.[9,10] The highest concentration of antibody in the regional node occurs about six or seven days following the injection of antigen. Lymphocytes later carry antibody into the general circulation. When the dose of antigen exceeds optimum, the reaction becomes one of frank local inflammation with hemorrhage, necrosis, and even suppuration either at the injection site or at the regional lymph node. Sometimes general reactions of the vascular connective tissue result, especially following intravenous injection of bacillary antigen or following the injection of foreign serum antigen.[11] The lesions are most prominent in the lungs, spleen, and liver. When moderately large doses of vaccine are injected, the thymus almost immediately decreases in weight and then becomes hyperplastic. Shrinkage of the thymus occurs prior to antibody production and is indicative of a non-specific injury reaction, the alarm reaction of Selye. Since Selye[12] showed that many different varieties of trauma can eventually result in vascular lesions, it remains to be seen to what extent adrenal cortical hormones condition vascular response due to severe immune reac-

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tion stimulation. The borderline between local damage to the recipient of an immunizing bacterial antigen and optimal stimulation is not sharp. Experimentally, the appearance of lymphocytes and plasma cells in the intima and adventitia of vascular tissue during exposure to antigen is indicative of good antibody production, whereas the appearance of monocytes and histiocytes indicates that the stimulus of the antigen was excessive.[8]

Clinically, the current trend is toward the use of a number of immunizing antigens in mixtures, and to their use early in infancy. Undesirable clinical reactions are no greater for diphtheria-tetanus-pertussis vaccine combinations than for immunization with diphtheria toxoid alone. The antibody response, particularly for diphtheria toxin, is even enhanced when the several antigens are used.[13,14] The antibody response to simultaneous injection of six specific polysaccharides of pneumococcus is as good for each of the six antigens as the response when the polysaccharides are administered singly.[15] Antibody response is also enhanced by the use of slowly soluble antigens (alum-precipitated toxoid for instance) or by making the antigen more slowly available in the tissues through water in oil emulsion, aquaphor, or similar carriers, Sometimes killed tubercle bacilli are added to such a menstruum further to reinforce antibody response to a specific antigen.[16] It has been held that infants under six months of age do not respond satisfactorily to antigen stimulation. But the new evidence is that the antibody response, while not quite as vigorous or as long lasting as that of older infants, is still adequate even in the first weeks of life for effective protection.[17,18] Further, it is these youngest children who have the highest mortality rate from pertussis. The first dose can even be given before the newborn leaves the hospital.

Another field of applied immunology is immunization with BCG vaccine which has now been administered to over one half million tuberculin negative persons since 1940. Vaccination of tuberculin negative persons with BCG has proved to be safe, to cut mortality from tuberculosis to a quarter of the expected rate, and markedly to decrease morbidity in those less completely protected.[19,20] Until antibiotic research gives us a more potent weapon against this plague, BCG remains our most effective tool.

Of general clinical interest are reports that severe nutritional deficiences of protein,[21] or, even more spectacularly, of pyridoxine[22] impair antibody production in rats. Deficiency in riboflavin, thiamin, or pantothenic acid severe enough to impair growth does not diminish antibody response.

Red Blood Cell Factors

The blood grouping factors are interesting clinically because of their practical applications in transfusion and in the genesis of erythroblastosis foetalis. Immunologically, they are of special interest, because the antigens involved are inherited.

Fetal agglutinogens (antigens of the red cells) are recognizable by the thirty-seventh day of intrauterine life and reach maximal levels when the individual is 20 years old. This level is then maintained for life. Antibodies in the serum (agglutinins, hemolysin) occur naturally in the globulin fraction of plasma when the corresponding A or B red cell antigens are absent. These antibodies appear about 10 days after birth, increase until puberty, and then slowly decline. Serum agglutinins present before the tenth day are maternal in origin. For this reason, except in instances of erythroblastosis foetalis where maternal serum antibody is the pathogenic agent, a mother's blood will be tolerated by her own infant.[23]

Red cell antigens excite the formation of antibody readily, but only when injected into individuals not naturally possessing the same antigen complex. The reason for this immunologic curiosity has been found to be the existence of inhibitors. These are polysaccharides and are found in greatest concentration in the stomach, pancreas, and salivary glands. In a person with type A red cells, there are inhibitors for type A antibodies. A different carbohydrate is found in persons with B type red cells, and this inhibits antibodies for B factor. An O-specific substance has been reported in the gastric juice of persons belonging to group O. Group specific substances have also been found in commercial pepsin, peptone, and rabbit erythrocytes.[23] Further, pneumococci type XIV and extracts of hog and horse stomach contain A, B, and O antibody inhibitory factors.[24,25] Group specific substances are thought to protect the fetus when its blood group is incompatible with that of its mother, since they inhibit antibody elaborated by the mother in response to fetal red cell antigenic stimulation. They also inhibit any antibody which might be elaborated by the fetus to its own antigenic red cells. Polysaccharide inhibitors may be added to group O blood to inhibit serum antibodies when it is desired to give this type of blood to persons of other blood groups.[26,27]

A variety of red cell factors are now known. Group A has been broken down into three subgroups, A_1, A_2, A_3. There are no subgroups of B factor. Erythrocytes also contain either M, N, or MN factors which are fully developed at birth.

Rarely, factor N^2 is found. The MN factors are poor antigens and are chiefly of value in disproving paternity.[23] Seventy-five percent of erythrocytes in the white race contain factor P which is weakly antigenic. Cold agglutinins, the presence of Wharton's jelly from the umbilical cord, and agglutinins associated with bacterial contamination of cell suspensions may give "false positive" agglutination in cross matching for transfusions.[28]

There are three principal Rh factors known (Rh_0, Rh_1, Rh_2) and three principal Hr factors (Hr, Hr,′ Hr″). These are antigenic upon their introduction via transfusion or pregnancy into an individual who does not naturally possess them, and are important both because they can give rise to erythroblastosis foetalis and because they can cause transfusion reactions. Erythroblastosis due to A and B factors is rare but has also been reported.[29,30] Erythroblastosis foetalis occurs usually when a woman lacks the Rh factor and is pregnant with an Rh positive fetus. The fetal red cells are antigenic and stimulate the mother to produce antibody. Maternal antibody diffuses through the placenta, coats the fetal red cells, clumping and destroying them and giving rise to the various pathologic features of the disease. Maternal antibody levels usually do not become high enough to damage the fetus of the first pregnancy. Transfusion of Rh positive blood into Rh negative females can stimulate antibody formation and a first pregnancy may then be disastrous for the child. Repeated Rh positive pregnancies in an Rh negative woman excite progressively higher antibody responses, with the eventual development of erythroblastosis and miscarriages increasingly early in pregnancy. Following the birth of an erythroblastotic infant, it is especially important to study the red cell factors (Rh and Hr) of the husband and other children to determine whether an Rh negative baby might be conceived. *Warning:* Rising maternal Rh antibody titers in pregnancy may occur nonspecifically when an Rh negative baby is carried.[31] The baby will not be harmed by this, of course. The rising titer should not be considered an infallible indication for early operative intervention.

Anaphylaxis

Frankly undesirable are those antibody reactions classified as anaphylaxis, bacterial sensitivity of tuberculin type, serum or drug sickness, contact-type dermatitis, and atopy.

Anaphylaxis, for technical reasons, is a term best restricted to experimentally induced phenomena in laboratory animals, although in current inexact usage it is applied both to accelerated serum sickness reactions and to atopic constitutional reactions. True anaphylactic reactions are mediated by precipitin antibodies. Precipitin antibodies are demonstrable in man but have never been linked with allergic reactions in man. Anaphylactic reactions are influenced by antihistamine medications. However, the survival rate of animals subjected to anaphylactic shock following antihistamine therapy is only about one-tenth that expected for comparable histamine poisoning.[32,33] Some believe that histamine release in anaphylaxis is intracellular and that the drug does not reach the histamine before the cell is poisoned. Others believe that substances other than histamine are largely responsible for anaphylaxis, as, for instance, the enzymes protease[34] and fibrinolysin.[35]

Tuberculin Type Allergy

Bacterial sensitivity of the tuberculin type is widespread for both ordinary and virulent bacteria, fungi, and, in some instances, viruses. The antigen is found in dead bacteria and molds as well as in living ones, and the cutaneous excitant also is present in bacteria-free filtrates. The filtrates, however, do not act as complete antigens for they are unable to sensitize. The lesion in a sensitive animal is productive, beginning with round cell infiltration, and appears grossly, 24 to 48 hours after the cutaneous application of the antigen. All varieties of cells, not just lymphoid cells or smooth muscle or vascular endothelium, are directly affected by the antigen. Such sensitized cells may undergo necrosis when antigen is added to them in tissue culture, even though the culture medium contains no antibody.[36] The injection of tuberculin into an individual infected with tuberculosis has long been recognized as a hazardous procedure, for in very sensitive cases the local productive tissue reaction around the bacteria serves to disseminate them. This is why in man, even skin testing is commonly carried out with a weak solution, as the PPD No. 1, prior to the intracutaneous injection of the full strength test solution. Tuberculin injection is an old-time non-specific treatment for bronchial asthma, but has been abandoned because of the danger of activating quiescent tuberculosis. Tuberculin-like antigens of clinical usefulness are: histoplasmin, coccidioidin, epidermophytin, brucellergin, chancroid vaccine, and the Frei test for lymphopathia venereum. Cutaneous reactions to the common bacteria and molds are almost universal, and the pathologic significance of these reactions must be carefully weighed before the organisms in question are labelled causative of any particular disease process. The antibodies formed do not circulate in the serum but are intracellular in blood cells, in cells of peritoneal exudate, and in parenchyma of liver and spleen.

Until very recently, tuberculin-type sensitivity could be initiated only by the injection of the whole bacillus, either dead or alive, or by actual infection. Tuberculin-type reactivity has been shown by Choucroun[37] and also by Raffel[38] to be inducible by a paraffin soluble protein from the tubercle bacillus. No immunity to infection is conferred by this purified sensitizer to tuberculin. Choucroun presents suggestive laboratory evidence that a paraffin and chloroform soluble polysaccharide ester of mycolic acid does enhance resistance to tuberculous infection, and this compound appears to be somewhat more effective when reinforced by the pure tuberculin sensitizer. At this point it might be again noted that a variety of killed bacteria and molds, as well as tuberculin, have been used nonspecifically as adjuvants to reinforce specific antibody formation. The efficacy of antihistaminics in influencing cutaneous hypersensitivity lesions to tuberculin have been variably reported. Sarber[39] states that, by administering these drugs to guinea pigs prior to tuberculin testing and continuously until the reaction was read, the inflammatory reaction was suppressed. Friedman[40] and other workers have been unable to confirm this. The effect of ACTH or cortisone on the tuberculin reaction has also been variably reported. Tuberculin type reactions do not persist for life. They diminish after the bacterial antigenic stimulus ceases, and quantitative tests have, therefore, some prognostic significance.[41] Of great theoretic importance are Raffel's[26,42] observations that sensitization of animals with the wax fraction of the tubercle bacillus in conjunction with either a simple chemical antigen, as picryl chloride, or a protein antigen, as egg albumin, can endow the picryl chloride or the albumin with the ability to elicit tuberculin-like reactions. Thus, picryl chloride, instead of inducing only its characteristic poison-ivy like reaction or anaphylactic shock, under these conditions elicits a tuberculin-type reaction quite independently of the other allergic responses. When egg albumin was injected into the corneas of animals, and the tissues were examined 48 hours later, thickening, necrosis, and cellular exudation were demonstrated in animals which had been sensitized with albumin plus tubercle bacillus wax and no change or only slight alterations at the needle puncture site were evident in the animals previously sensitized to albumin alone. (Since the cornea is avascular, Arthus' reaction was not present to confuse the issue). When bone marrow explants from animals sensitized to egg albumin alone were cultured and exposed to egg antigen, no adverse effect was noted. But bone marrow explants from animals sensitized to albumin plus wax were affected as to growth, cell migration, and even death of cells, when egg albumin was added. It would be unwarranted to translate these experimental findings in animals directly to man, but one certainly may speculate that bacterial infection might confer tuberculin-type antigenicity to foods and contactants. This might explain some of the so-called delayed or tuberculin-like reactions seen in the course of routine food skin-testing in man. The ophthalmologist will also recognize the possible implications of this work in that field.

Serum or Drug Sickness

Serum sickness is a syndrome excited either by the injection of foreign serum protein or by the administration, orally or parenterally, of drugs. "Sulfa drugs" and penicillin are now common excitants. The reaction is most common after repeated use of a foreign serum or drug but may follow the first administration of foreign serum or a drug after an incubation period of from one week to more than three weeks. Antigenic dye has been found to remain in tissues up to three and a half months.[5,7] If the drug or serum has been administered previously, an accelerated reaction may appear in a matter of hours. The symptoms consist of one or more of the following: fever, rash (urticaria, scarletiniform, morbilliform, erythema multiforme, etc.), joint pains and tenderness, edema of the face and dependent parts, and occasionally wrist drop or other evidence of peripheral neuritis. There is no skin test to detect susceptibility to the serum sickness type of reaction or to decide which of several drugs administered caused the reaction. Occasionally, skin sensitizing antibodies of the type found in hay fever are formed, and precipitin antibodies are also of irregular occurrence, but neither antibody has been correlated with the appearance or nonappearence of the disease.

Rich and his co-workers[43] have presented some fascinating findings. In eight successive fatalities in patients who developed serum sickness to serum or sulfa drugs or both, fresh lesions of periarteritis nodosa were found at autopsy. One particularly conclusive case was that of a man who was given sulfathiozol prophylactically following biopsy of his scrotal carcinoma. A week later he had typical serum sickness. The drug was continued because of his fever, and he died nine days after the onset of his serum sickness. Autopsy disclosed widespread fresh lesions of periarteritis nodosa. Moreover, the biopsy specimen taken at his last operation, as well as another which had been taken five months prior to death, showed no evidence of periarteritis. Following this experience, Rich injected horse serum

into rabbits and observed periarteritic lesions, lesions in the heart suggestive of rheumatic fever damage, involvement of renal vessels, and pulmonary lesions "with the basic characteristics of rheumatic pneumonitis."

Hawn and Janeway[44] conducted a classic experiment. They injected highly purified bovine serum albumin, bovine serum gamma globulin, or whole sterile bovine serum intravenously into rabbits. They discovered that the albumin-injected rabbits developed lesions which were maximal two weeks after the injection, at a time when antigen was still in the circulation and when precipitin antibodies were just appearing. The lesions involved the intimal and subintimal coats of pulmonary and mesenteric arteries, and the great vessels of the heart and valvular endocardium. One animal exhibited mild glomerulonephritis and lesions "resembling Aschoff bodies." The glomerular lesions healed with occasional scarring and the arterial lesions healed without scarring. Whole bovine serum produced more intense reactions, principally like those of the serum albumin alone. Heyl and Janeway[45] administered crystallized bovine albumin to sixty humans. Twenty-four developed serum sickness. The manifestations included purpura, signs of hepatic and renal damage, and cardiac symptoms with electrocardiographic changes. One subject died and autopsy disclosed necrosis of the myocardium. In contrast to the findings in rabbits, precipitins were not prominent in these subjects, appeared variably, and sometimes could not be demonstrated at all, even in the presence of serum sickness. More[46] in carrying out experiments which verify the above work, considered that the cardiac lesions induced by bovine serum gamma globulin were very similar but not identical to those seen in rheumatic fever in man.

A somewhat different line of approach was followed by Cavelti[47,48,49,50] to produce rheumatic fever-like lesions in the heart and glomerulonephritis-like lesions in the kidney. He followed the lead of other workers who mixed staphylococcus toxin with lens substance, muscle tissue, kidney, or skin of the same species used for experimentation. Such a mixture induced antibodies in an animal to his own tissues (whichever tissue had been injected with the toxin). The antibodies were therefore called autoantibodies. Cavelti injected rabbits and rats with emulsified rabbit or rat tissues respectively, plus killed streptococci. When the tissue emulsion consisted of heart or connective tissue, the animals developed changes in their cardiac connective tissue and heart valves suggestive of rheumatic fever. Attempts to repeat this work have, however, thus far been unsuccessful.[51] Murphy and Swift[52] injected live group A streptococci repeatedly into the skin of rabbits over a period of months. The animals developed myocardial lesions very similar to those found in human rheumatic fever. Controls including those immunized with groups A or C streptococcal vaccines did not manifest these lesions. One wonders whether the active infection in the skin has not resulted in some degree of emulsification of connective tissue which, in the presence of the streptococci, in effect repeats the Cavelti experiment.

When Cavelti substituted rat kidney for heart tissue in his experiments, nephritis was noted one to two weeks after the completion of immunization. Most rats recovered within a few weeks. A few died of azotemia. Some went on to a subacute stage of nephritis which became chronic after many months. The clinical picture was confirmed histologically. Rat kidney emulsion injected independently of the streptococcic vaccine did not cause nephritis and only rarely did injection of killed streptococci alone (in repeated, very large doses) eventuate in nephritic lesions. More data on human subjects is supplied by Lange and his co-workers[53] who coated collodion particles with an extract of human renal tissue and watched for agglutination of these particles by various sera. Twelve patients who had had glomerulonephritis for less than one year were found by this technique to have an average renal antibody titer of 1:918. Eleven patients who had had glomerulonephritis for more than one year had titers averaging 1:337. Seventy-five percent of the 112 tests run on these patients showed agglutinating antibody for human kidney. Of 68 controls, 19 percent had agglutinating reactions, the average titer being only 1:78. The glomerulus apparently contains the most potent antigen in renal tissue. When antibodies for mouse kidney were subjected to iodination by radioactive iodine[54] and then injected into normal mice, the pattern of distribution of the antibody was found to be that of the glomeruli.

In all of the above work one must not lose sight of the very similar heart, kidney, vascular, and even joint lesions produced by a wide variety of stress factors which, as far as we know, are quite unrelated to immunologic mechanisms.[12] It is possible that immunologic reactions act via pituitary and adrenal cortex as one form of stress, and that in the case of antikidney antibodies kidney is predisposed to stress type injury as a result of the local kidney cell-antikidney antibody reaction.

Contact Dermatitis

Contact-type dermatitis can be induced in anyone following sufficiently prolonged exposure to certain antigens. There is no known familial predisposition

to sensitivity in humans, although animals may be bred selectively for the trait of ease or difficulty of sensitization. A minority of people readily become sensitive to such things as adhesive plaster, common dress dyes, leather hat or watch bands, rubber gloves, or nylon stockings. On the other hand, paraphenylene-diamine dye, poison ivy, and certain tars and resins used industrially are notorious sensitizers. Other typical contactant antigens are simple metal salts, formaldehyde, essential oils, drugs, plant oils, dyes, plastics, and sizing materials. Ordinarily, sensitivity is induced by repeated cutaneous contact, and the reaction is provoked by cutaneous contact. However, locally applied medicaments are frequent causative allergens and their ingestion or injection, subsequent to skin sensitization, can lead to reactivation of the old skin lesions. Antibiotics, sulfa drugs, and now antihistaminics are particularly apt to be offenders in such a chain of events.

Recent studies by Rostenberg and Kanof[55] indicate that specificity extends to very close chemical relatives of the original sensitizing agent. The body fails to distinguish between chloride and bromide atoms, for instance when they occupy the same relative positions on a benzene ring. The capacity of the skin to react is progressively diminished as testing is carried out with compounds dissimilar to the compound used to sensitize the skin.

The incubation period during which antibody is built up to clinically reactive levels varies from a few weeks to many years. The principal seat of reaction is probably either in the superficial and epithelial portion of the skin or the immediately underlying vascular bed. Microscopically, the lesion consists of spongiosis, vesicle, and papule formation. Sensitivity may remain sharply localized at the principal site of contact for months or may extend to involve the entire skin. This fact must be kept in mind when patch tests are applied in the hope of detecting the causative agent. Patch testing close to the lesion is more apt to be successful than testing at a distance. A positive patch test reaction *to a substance other than a primary irritant* is always highly significant, for it is a typical clinical exposure in miniature. A negative patch test, however, may simply mean non-extension of sensitivity to the area used for the test.

The best treatment for contact-type dermatitis is bland applications, protective covering, and, above all, avoidance of the causative agent. Antihistaminics, occasionally, and local anesthetics, more regularly, relieve the itching, but both are themselves potent contact type sensitizers, and the ability of a contactant to sensitize is enhanced both by the existence of broken skin and by the previous allergic response of that area.[56] Injection treatment for contact dermatitis is still, after years of trial, not of proved value, and may cause serious flare-up of the sensitized skin. Carefully applied irradiation may be beneficial, and ACTH or cortisone have been reported of value in a very few cases. These potent hormones have usually been withheld in favor of simpler and safer therapy.

Atopy

Atopy is that subdivision of allergy which is characterized by an inherited predisposition, skin sensitizing antibody (responsible for the immediate wheal reaction of the skin), eosinophilia locally or in the blood, an edematous lesion at the site of reaction, and a benign, chronic course. More than one of the following manifestations often appear in a single patient: atopic eczema, hay fever, asthma, vasomotor rhinitis, vernal catarrh, atopic neurodermatitis, angioneurotic edema, urticaria, migraine, and a variety of gastro-intestinal symptoms.

A significant advance in this field has been the development of antihistaminic drugs for symptomatic control. Their effectiveness underlines the importance of histamine release in the mechanism of the atopic reaction. Wells and his associates[57] have presented evidence that Benadryl is absorbed onto the site of action of histamine. Histamine release is not, however, the entire story, and the basic process is still poorly understood. Asthma is responsive to these new drugs in only about 20 percent of cases, and, on occasion, is made more severe by their use. Benadryl causes bronchial constriction in isolated lungs[58] and, in the experimental animal, causes shallow, rapid respiration by way of carotid and vagal reflexes.[59] Benadryl and pyribenzamine have a potent atropine-like action also and thus contribute to plugging of bronchi with thick mucus in asthmatics. Epinephrine is still the drug of choice for severe asthma and other allergic emergencies. The place of ACTH and cortisone is discussed separately later. In atopy, as in drug (serum) sickness and contact dermatitis, the best treatment remains identification of the responsible allergen and avoidance of it. Hyposensitization to the inhalent allergens when they are offenders is the second choice in treatment, and non-specific treatments such as vaccine, histamine, and "dust" injections rate third. Symptomatic treatment of symptoms as they arise is a poor fourth choice but still preferable to a grin-and-bear-it regime.

Even though atopy is an inherited ailment and the genetic pattern once set cannot be changed, much can be done to minimize and to prevent the

clinical manifestations of this disorder. The first step in prevention is early recognition that the patient is atopic. "Just a touch" of hay fever, eczema, or asthma stamps an individual as one who has inherited the atopic trait. It has been estimated that approximately one in four children will "outgrow" asthma at the time of puberty even if nothing is done to help them. The number of remissions can be increased one- or two-fold, however, by good allergic management (removal of allergens, specific hyposensitization to unavoidable inhalents). Infantile eczema of atopic type will clear in a majority of cases within about three years, but the incidence of bronchial asthma following this is very high. It has been variously estimated at from 70 to 90 percent. We do not know why allergic manifestations appear when they do, why an individual may go along without difficulty for years with allergic antibody demonstrable to ragweed and then finally develop ragweed hay fever. But we do know that an allergic reaction tends to perpetuate itself and that additional sensitivities are most apt to be developed during periods of allergic upset. For instance, a seasonal asthma, as that due to ragweed, is at first limited to the ragweed pollination season. Frequently the next step is persistence of the asthma a month or two beyond this time and recurrence with upper respiratory infections. Then the next step, all too often, is the extension of the asthma throughout the year, at which point the patient is found sensitive to many things other than ragweed. This chain of events is largely preventable. Deformed chests due to childhood asthma are often preventable. Nasal polypi and chronic sinusitis, which so often follow on the heels of allergic rhinitis, can often be prevented by control of the underlying allergy. On the eastern seaboard about 30 percent of cases of untreated ragweed hay fever develop seasonal bronchial asthma as a complication; in the Midwest this figure is nearer to 60 percent. Hyposensitization cuts the incidence to nearer to 2 percent.

There are some general measures which can be taken as soon as a child shows evidence of atopy. Early immunization to the infectious diseases is advisable because pertussis often ushers in bronchial asthma. Vaccination should be carried out early, if possible, before the presence of atopic eczema contraindicates this procedure. In the older child it is reassuring to know that there is active tetanus immunity so that, in the event of an injury, one need never be forced to administer anti-tetanus horse serum under difficult circumstances. Nose and throat operations should not be performed during spring, summer, and fall, while pollens are in the air, if this can be avoided. Hay fever antibodies may be present for years in the blood stream and operative trauma often initiates the clinical manifestations of hay fever. Much in the same category is the prevention of upper respiratory infections by making reasonable efforts to separate the individual from other persons having fresh colds. When a cold is contracted, antihistaminics should be given a trial for controlling the drippy stage and blockage; and, if bronchitis develops, iodides given as syrup of hydriodic acid, in the child, and saturated solution of potassium iodide, in the adult, will help to drain the infection from the bronchial tree. Aminophyllin and ephedrine are also useful in the management of bronchial infections in the pre-asthmatic. Antibiotics are, of course, useful, but since they are frequent allergen offenders they should be used only where really necessary. All atopic children, regardless of their present sensitivities, and inhalent sensitive adults deserve the protection of a dust-free bedroom. For many patients this means simply that water-proof encasings are put on all pillows, mattresses, or other padded furniture in the room, or rubber foam furnishings are substituted for stuffed things. Mothballs and crystals are eliminated because of their irritant effects on nasal and respiratory mucosa. Cleaning is done by dampened cloth or mop only. If the housewife is sensitive to dust and must do her own cleaning she can be helped by wearing a large dampened handkerchief over her mouth and nose. The bedroom is the chief point of attack because 8 to 10 hours are usually spent there. Offices, school rooms, and outside air are usually devoid of the harmful feather and "overstuffing" dusts.

The commonest food allergens are the dietary staples. Feeding a food frequently probably favors the development of allergic response to that food. It is considered advisable to feed the atopic child as varied a diet as possible. Cereal foods consisting of a mixture of cereals are thus not desirable and are easily avoided in favor of oatmeal, rice cereal, barley cereal, and plain wheat cereals. Dietary sprees should be discouraged. The writer likes to keep a basic diet of foods never fed to the child (such as pork, rye, pineapple, and a green or yellow vegetable) in reserve. If the child has never had these foods in his own diet or in his mother's diet, if she nurses him, he cannot develop allergy to these foods. Then, should the child develop eczema or other signs of allergy, it is relatively easy to clear up the symptoms by placing him on the safe foods. The regular foods are then added back and the offenders identified.

There are important psychologic gains involved in stopping allergic reactions as early as possible. The person suffering from asthma, hay fever, diarrhea, or migraine is not a well person. He is un-

comfortable, often fatigues easily, and, if the symptoms are severe, lives under a cloud of dread of the next attack. Children often express their discomfort by becoming drowsy, by muscular hyperactivity, by quarrelsomeness, or by tantrums. No one lives in a social vacuum, and these reactions and emotions are reflected on those surrounding the allergic. The allergically upset man who snaps at his wife as he leaves in the morning is apt to get a cool reception on his return that night. Siblings react to seeing the sickly child favored. Parents often become really fatigued when their sleep is frequently interrupted and are more on edge with each other and the children, too, than they would otherwise be. If the lesion is eczema, parents avoid showing off their baby to relatives and friends and feel a sense of guilt. It is no wonder that victims of atopy have psychologic problems!

Cortisone and ACTH

The effects of the hormones ACTH and cortisone have been of particular interest to allergists and immunologists, because of their profound clinical effects in atopy and because of their dramatic effects in such diseases as lupus erythematosus and rheumatic fever, which have for so long been suspected of having an allergic etiology. It must be noted here, however, that on the one hand the scope of these drugs extends far beyond their "anti-allergic" activities, as, for instance, their efficacy in the treatment of burns, and on the other hand these hormones have little or no effect on some well-established allergic mechanisms, such as anaphylaxis,[60,61] excepting possibly anaphylaxis in the mouse.[62] Neither is effective in counteracting the Arthus reaction which accompanies the anaphylactic state. Cortisone and ACTH are still relatively recent additions to the medical scene and there is not yet general agreement on all phases of their effects. Reports are variable as to the effect of these hormones on circulating protective antibody levels. Precise quantitation by Bjorneboe and his associates[63] using pneumococcal vaccine in rabbits and measuring antibody as specific antibody nitrogen discloses a drop in circulating antibody levels. The degree of fall is such that it could easily be missed by usual techniques. It is interesting that the fall may occur as soon as a few hours after the first dose of cortisone. Since the half life of antibody protein is about two weeks, Bjorneboe suggested that actual destruction of antibody protein might be taking place. The pathologic picture of cortisone-treated immunized animals was that of atrophic malpighian bodies with fragmentation of lymphocytes in the splenic follicles and, in general, reversal or inhibition of most of the alterations observed in hyperimmunized controls. It should not be forgotten that this work, while of excellent caliber, still was carried out in rabbits, and that there are species differences in physiologic and pharmacologic reactions. Massell and his co-workers [64] reported no effect of ACTH, 30 mg. daily, on the antistreptolysin O titer and gamma globulin response in scarlet fever victims. Acute glomerulonephritis developed in 2 of 10 cases so treated and in one of 10 controls. One might argue that the dose was insufficient or that the technique for measuring antibody was too crude, but it also might be that man will not show quite the same responses as the rabbit. It will be well to keep an open mind until further data appears. Human responses to intercurrent infections are greatly altered by the administration of these hormones. Individuals with pneumonia or tuberculosis become afebrile; patients may perforate a peptic ulcer and die of peritonitis without evidence to make one suspect such an illness. One of the great dangers of these drugs is the masking of conditions which require attention. There is some question as to whether quiescent tuberculosis may be flared up to activity by hormonal therapy or its discontinuance.

The effect of ACTH and cortisone on the tuberculin skin test reaction is another unsettled point. Fischel[65] found no reduction of tuberculin reactivity in 10 of 12 patients and the 2 having diminished or obliterated reactions showed other skin changes along with hyperadrenalcortism. He also reported no change in human reactivity to streptococcus nucleoprotein (C18 K fraction of Heidelberger and Kendall). Stoerk[66] and others have reported directly conflicting results. Sulzberger[66] reported two cases in which persons having negative cutaneous reactions to tuberculin prior to ACTH administration became tuberculin positive under therapy. He concluded that the tuberculin response was variable in either direction. The writer has seen evidence that the tuberculin-like reaction to Ascaris lumbricoides antigen is suppressed by cortisone in its early stages of development, but when sensitivity becomes more intense the delayed reaction is no longer masked.

Red cell antigen reactions may be somewhat depressed by the administration of ACTH or cortisone. Palmer and his associates[67] report that when a relatively large amount of anti-red cell antiserum was given to rats in small doses both ACTH and cortisone prevented the development of anemia. Large doses of antibody, however, were not counteracted. Gardner[68] has treated three clinical cases of acquired hemolytic anemia with favorable results.

Serum reactions in animals were intensively studied by Wedgwood, Hawn, and Janeway[69] using bovine serum gamma globulin in rabbits. Treated rabbits produced antibody at rates comparable to the controls, and combination of antigen with antibody and complement proceeded identically in treated and control groups. The one great difference noted was that the treated animals failed to develop glomerulonephritis lesions and the controls developed extensive lesions. In other words, ACTH blockage effect occurred at the tissue injury level and not by interfering with the production of antibody or the interaction of antibody and antigen. Several reports are available of complete relief of serum sickness with these drugs.[70,71] The writer witnessed one dramatic response of serum sickness to horse serum tetanus antitoxin in which the patient was experiencing edema of the larynx and receiving adrenalin once an hour. One dose of 200 mg. cortisone gave complete relief and no further adrenalin was necessary after the cortisone was administered.

There is relatively little information as to the effect of the cortical hormones on contact dermatitis. Sulzberger[66] reported that patch tests in one sensitive case of poison ivy elicited a weaker reaction during and for a short period after the administration of ACTH. Two patients with strongly positive reactions to paraphenylenediamine and to leather maintained approximately the same reactions under ACTH treatment. Cooke[72] believed that one of his cases was more rapidly relieved of acute contact dermatitis than would be expected without hormone therapy.

There is widespread agreement that ACTH and cortisone produce clinical remission in a large proportion of sufferers from asthma, hay fever, urticaria, and eczema, but that this effect is not permanent. Remission in Shulman's series of asthmatics lasted for 54 days (median).[73] The titer of allergic antibody remains unchanged. Most observers agree that skin reactivity to histamine and to specific antigens in most individuals is unchanged during therapy. To investigate the effect of allergens on the shock organ itself Feinberg[70] did tests of eye and nasal mucosa reactivity in hay fever patients. Only one of 9 patients showed increased tolerance of her shock organs for ragweed antigen while receiving ACTH. Grob and his group[74] carried out vital capacity studies in asthmatics and found that ACTH protected against inhalation of specific pollen or spore offenders but did not counteract aerosolized inhaled histamine, histamine administered intramuscularly, or mecholyl given intramuscularly, despite doses of ACTH sufficient to cause remission of the subject's clinical asthma. These workers concluded that the effectiveness of ACTH in asthma was not mediated through alteration in reactivity to a cholinergic substance and probably not directly mediated through reactivity to histamine or release of histamine from tissues. We do not know yet why these drugs favorably affect the atopic illnesses. We do know that they may be life saving in an emergency. Shulman[73] has not found that repeated courses are in any way diminished in effectiveness over the original course. Rose,[75] however, has reported decreased effectiveness in control of asthma on repetition of courses of ACTH. Shulman recommends that a minimum of 500 to 800 mg. of ACTH be given over a period of from 10 to 15 days to obtain a maximal period of remission. It is quite generally agreed that these hormones are useful as stopgap therapy, but earnest search must be made for the causative allergens in all chronic cases of allergy. Caution: several cases of allergy to ACTH of pork origin have been reported.[76] Beef ACTH has been tolerated by these patients, but of course it is also potentially allergenic.

Summary

The field of allergy is reviewed with regard to some of the recent discoveries, and present day concepts are outlined. A classification of allergy is presented. The current status of cortisone and ACTH in allergic mechanisms is briefly reviewed.

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CASE REPORTS

UNUSUAL POSTPARTUM COMPLICATION

Josephine E. Renshaw, M.D.

A DRASTIC REDUCTION in maternal mortality has been achieved during the past two decades, from a plateau above 60 per 10,000 live births before 1930 to a level of approximately one fourth that rate in 1946.[1] This has been accomplished not only by better prenatal care but also by better care in the puerperium. Puerperal infection remains, however, one of the three leading causes of maternal deaths, in spite of modern drugs and ready availability of blood. Eastman[1] has warned that "every fever in the puerperium should be regarded as due to puerperal infection unless proof positive can be advanced that it is the result of some extraneous cause." A case is reported here in which it was felt that the postpartum fever was indeed due to puerperal fever, but which turned out to be the result of "some extraneous cause." In order to give the reader an opportunity to exercise diagnostic acumen, the findings are not given until the end of the case report.

CASE REPORT

The patient was a 31-year-old white para O, gravida 1, whose last menstrual period was October 31, 1949, making her estimated date of confinement August 7, 1950.

Her past history was non-contributory. Her menstrual periods began at the age of 11, occurring every 28 days, lasting five days. She occasionally had dysmenorrhea. She was married on August 6, 1949, used no contraception, and became pregnant in November. Pelvic examination at the first prenatal visit was entirely normal, and her prenatal course was uneventful except for nausea and vomiting in the early weeks.

Membranes ruptured spontaneously at home at 9:00 a.m. on August 8, 1950, but the patient was not admitted to the hospital until 4:30 a.m. on August 10, which was an hour and a half after the onset of labor. Because of her admission temperature, 100.6 F., she was given 300,000 units of penicillin. After 12 hours and 35 minutes of labor, she was delivered of a 6 pound, 11 ounce female infant by low forceps over a right mediolateral episiotomy. The baby was covered with a foul smelling discharge, but was otherwise in good condition and breathed and cried spontaneously. Since the placenta did not separate readily, it was removed manually.

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Following delivery the patient received 400,000 units of penicillin daily. Her temperature, pulse, and respirations remained normal until the afternoon of the third postpartum day. Just 72 hours after delivery she had a sudden onset of chills, at which time her temperature was 102 F., pulse 105, and respirations 24. She was started on gantrisin. 1 Gm. every 4 hours, in addition to the penicillin. After two days, temperature, pulse, and respiration returned to normal, but the patient was nauseated and vomited. There was no abnormal distention, but there was marked rebound tenderness over the lower abdomen. It seemed likely that the patient now had a pelvic peritonitis following her intrapartum infection. She was given nothing by mouth and received adequate intravenous therapy, but the vomiting persisted. The gantrisin was then discontinued and streptomycin 0.5 Gm. every 6 hours substituted. She improved considerably and had no further vomiting, but the abdomen remained tender. On her sixth postpartum day she received 500 cc. of whole blood and again took nourishment by mouth. For two days she appeared to be improving. However, on the evening of August 18, her eighth postpartum day, she was crying with pain in the upper abdomen. There was still no abdominal distention and an enema was effectual. Pelvic examination at this time showed no induration, swelling, or tenderness. The white cell count was 18,500 and showed a shift to the left.

A few hours later the abdomen showed distention for the first time. There was generalized tenderness, most marked in the right lower quadrant. Peristalsis was both audible and visible, moving from left to right. X-rays confirmed the tentative diagnosis of small bowel obstruction. Wangensteen suction was started; intravenous fluids were given, and the patient was prepared for surgery. At operation, the patient was found to have chocolate cysts of both ovaries, the right one having already ruptured, the left one measuring 6 cm. in diameter. The small bowel was adherent in four different places to the spilled contents. After the bowel had been carefully freed it looked relatively healthy and no resection was necessary. The right ovary was removed and the abdomen closed.

The postoperative course was relatively uneventful, and the patient was discharged on her twentieth postpartum, and eleventh postoperative, day.

When last seen, five months following delivery, the patient was in good condition. The left ovary was about twice normal size, but periods were occurring regularly and giving no trouble.

It is our opinion that the sudden onset of chills and fever on the third postpartum day was due to rupture of the right ovarian cyst, and that complete intestinal obstruction did not occur until a few hours prior to the operation.

DISCUSSION

Endometrial cysts complicating pregnancy are exceedingly rare. Rupture of these cysts are even

more rare. Scott[2] in 1944 reported two cases of rupture of endometrial cysts in pregnancy. He made a thorough search of the literature but was unable to find a report of any similar case. In both of his cases the rupture occurred prior to term. In 1946 Burger[4] reported a case similar to Scott's. To our knowledge, no case has been reported where rupture of an endometrial cyst occurred in the puerperium. In addition to reporting his two cases, Scott gives an excellent discussion of endometriosis in pregnancy. We recommend his paper strongly to anyone interested in the subject. The following quotations from it are of interest.

"Ovarian endometriosis, the second most commonly reported type found during pregnancy, can be clinically recognized in several ways. The cyst may produce symptoms because of slow and occasional leaking, produced not by intermittent hemorrhage into the cyst with increased tension but by increased counter tension by the enlarging uterus upon an already tense cyst. Endometrial cysts are usually adherent and consequently less amenable to intra-abdominal adjustment. Because of these adhesions, too, they seldom twist. Rupture of these cysts may cause a dramatic episode of acute abdominal pain and extensive peritoneal irritation." "Ovarian endometriosis complicating pregnancy was reported seven times in the literature" "Undoubtedly, many patients with asymptomatic endometriosis, minimal or moderately extensive, have uncomplicated antepartum, intrapartum and postpartum courses."

Lock and Myers[4] in 1946 stated: "Analysis of five articles shows that approximately one third of the patients treated conservatively for endometriosis can successfully conceive, and indicates that the vast majority of such patients have a normal pregnancy."

Ware[5] in 1950 reported 13 cases in which pregnancy occurred in women with endometriosis. In 12 of these, pregnancy occurred following conservative surgery. In the thirteenth, the endometriosis was discovered at the time of Cesarean section.

Conclusion

Endometriosis and pregnancy do occur together frequently enough to warrant conservative treatment of endometriosis. And further, while endometriosis may become a complicating factor in a pregnancy, as illustrated in the above case report, this is an infrequent problem.

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INTRAVENOUS PROCAINE AND CURARE THERAPY OF TETANUS

Margaret E. Callan, M.D.

This report of a case of tetanus in which intravenous procaine and curare were administered in conjunction with other therapeutic measures is presented because it would seem that these drugs were of symptomatic value and that herein lies their usefulness in this disease.

Case Report

A 65-year-old colored man was admitted to Suburban Hospital on November 16, 1948, with a compound fracture of the right tibia and fibula by a flying tree stump. Debridement and plating were done at 6:00 p.m. on the same day, under nupercaine spinal and pentothal anesthesia. Blood, tetanus antitoxin, and gas gangrene antitoxin were given at the time of operation. Physical examination and analyses of the blood and urine were essentially negative. The postoperative course was uneventful. The patient was treated with penicillin and sulfathiazole daily until the seventh postoperative day, when he complained of difficulty in swallowing and in opening jaws and of stiffness of the neck muscles. He had no pain, however.

The diagnosis of tetanus was made and treatment with 50,000 units of tetanus-antitoxin intravenously and 1,000 cc. of 5 percent glucose-sodium chloride solution, with 1 Gm. procaine crystals added (0.1 percent solution), was started at once. The patient was at ease but unable to open his jaws. The following day the intravenous solution was repeated with 40 units of curare added, dripping at 20 drops per minute. The patient slept during the infusions and was generally relaxed, but the jaws were still tight. The following day the intravenous procaine and curare solution was repeated, and on the next day the procaine solution and 60 units of curare were given. The patient was at ease and slept at intervals. He showed definite improvement on the fourth day following the beginning of the tetanus.

Penicillin, sufadiazine, and tetanus-antitoxin every 8 hours, combined with tetanus-antitoxin and furacin ointment to the wound comprised the therapy. The patient was discharged as cured on December 27, 1948.

Dr. Callan is Chief of Anesthesia, Suburban Hospital, Bethesda, Maryland.

Conclusion

The improvement noted in the patient's general condition and in his comfort, when procaine solution and curare were added, points to the value of these drugs in the symptomatic treatment of tetanus.

Uniform Simultaneous Death Act

FACTS OF INTEREST TO THE PHYSICIAN

Irene Kennedy, LL.B.

THE UNIFORM SIMULTANEOUS DEATH ACT was brought before the meeting of the Conference of Commissioners on Uniform State Laws, in Philadelphia in 1940, and received the unanimous approval of all the States represented at the meeting, which were as follows: Arkansas, California, Colorado, Connecticut, District of Columbia, Florida, Illinois, Indiana, Iowa, Kentucky, Louisiana, Maine, Maryland, Michigan, Mississippi, Missouri, Nebraska, Nevada, New Jersey, New York, North Carolina, Ohio, Oklahoma, Oregon, Pennsylvania, Puerto Rico, Rhode Island, South Dakota, Tennessee, Texas, Vermont, Virginia, Washington, West Virginia, and Wisconsin. The Act was subsequently adopted by the legislatures of 37 states and Alaska. Maryland and Virginia adopted it in 1941.

Here in the District of Columbia we have no statute which provides for the administration of estates of persons who die in a common disaster under such circumstances that there is no evidence of survivorship.

The civil law indulges in various presumptions as to the survivorship between persons who perish in the same disaster, based on age, sex, and physical strength of the individuals, and the assumption was that the stronger would survive the weaker. But the presumption of the civil law in respect of survivorship extended only to parents and children and was founded on public policy, designed to keep inheritance in a fixed line of devolution. As between other persons, proof of survivorship was required as at common law. The French law made a distinction between the sexes, presuming in the absence of evidence that the male survived the female.

Mrs. Kennedy is a member of the American Bar Association and is admitted to practice in the United District Court for the District of Columbia, the United States Court of Appeals for the District of Columbia, and the Supreme Court of the United States.

The common law, which now applies in the District of Columbia, is that where two or more persons perish in a common disaster there is no presumption as to survivorship. In discarding presumptions and exacting evidence, the result is to put the burden of proving survivorship on any party claiming to derive title to property from the deceased person whose ownership during life depended on his outliving some other person also deceased, and the practical result is that, if the party on whom the burden of proof rests cannot make proof, his case fails. Therefore, in the absence of statute, it will not be presumed that one individual survived another, nor according to some authorities that they died simultaneously.

There is presently in the District of Columbia an absence of any orderly plan of distribution of estates in the case of simultaneous death. Our law does not cover such a situation. In the past the cases have been resolved by agreement where all the parties are *sui juris*. Where the parties or not *sui juris*, as in the case of minors or incompetents, it does not appear that the situation can be worked out by agreement.

Under our present way of living, families are more and more traveling together by plane, fast trains, and automobiles, and it is logical to assume that cases of simultaneous death will become more numerous. Thirty-eight jurisdictions have foreseen

the need for legislation and have adopted the Uniform Simultaneous Death Statute. There is a real need for legislation on the subject of survivorship, and steps should be taken to have Congress adopt the Uniform Simultaneous Death Statute for the District of Columbia.

The Committee on Uniform State Laws of the District of Columbia Bar Association has approved the adoption of the Uniform Simultaneous Death Act and, in a report, has recommended that the District of Columbia Bar Association take the necessary steps to have the Act enacted into law for the District of Columbia.

The Uniform Simultaneous Death Act reads as follows:

s 1. NO SUFFICIENT EVIDENCE OF SURVIVORSHIP. Where the title to property or the devolution thereof depends upon priority of death and there is no sufficient evidence that the persons have died otherwise than simultaneously, the property of each person shall be disposed of as if he had survived, except as provided otherwise in this act.

s 2. BENEFICIARIES OF ANOTHER PERSON'S DISPOSITION OF PROPERTY. Where two or more beneficiaries are designated to take successively by reason of survivorship under another person's disposition of property and there is no sufficient evidence that these beneficiaries have died otherwise than simultaneously, the property thus disposed of shall be divided into as many equal portions as there are successive beneficiaries and these portions shall be distributed respectively to those who would have taken in the event that each designated beneficiary had survived.

s 3. JOINT TENANTS OR TENANTS BY THE ENTIRETY. Where there is no sufficient evidence that two joint tenants or tenants by the entirety have died otherwise than simultaneously, the property so held shall be distributed one-half as if one had survived and one-half as if the other had survived. If there are more than two joint tenants and all of them have so died, the property thus distributed shall be in the proportion that one bears to the whole number of joint tenants.

s 4. INSURANCE POLICIES. Where the insured and beneficiary in a policy of life or accident insurance have died and there is no sufficient evidence that they have died otherwise than simultaneously, the proceeds of the policy shall be distributed as if the insured had survived the beneficiary.

s 5. ACT NOT RETROACTIVE. This act shall not apply to the distribution of the property of a person who has died before it takes effect.

s 6. ACT DOES NOT APPLY IF DECEDENT PROVIDES OTHERWISE. This act shall not apply in the case of wills, living trusts, deeds, or contracts of insurance wherein provision has been made for distribution of property different from the provisions of this act.

s 7. UNIFORMITY OF INTERPRETATION. This act shall be so construed and interpreted as to effectuate its general purpose to make uniform the law in those states which enact it.

s 8. SHORT TITLE. This act may be cited as the Uniform Simultaneous Death Act.

s 9. REPEAL. All laws or parts of laws inconsistent with the provisions of this act are hereby repealed.

s 10. SEVERABILITY. If any of the provisions of this act or the application thereof to any persons or circumstances is held invalid, such invalidity shall not effect other provisions or applications of the act which can be given effect without the invalid provisions or application, and to this end the provisions of this act are declared to be severable.

s 11. TIME OF TAKING EFFECT. This act shall take effect . . .

POSTDOCTORAL FELLOWSHIPS AVAILABLE

The National Foundation for Infantile Paralysis announces availability of a limited number of additional postdoctoral fellowships to candidates whose interests are research and teaching in medicine and the related biological and physical sciences. The purpose of these National Foundation fellowships is to increase the number of professional workers qualified to give leadership in the solution of basic and clinical research problems of poliomyelitis and other crippling diseases.

The fellowships cover a period of from one to five years. Stipends to Fellows range from $3,600-$7,000 a year, with marital and dependency status considered in determining individual awards. Institutions which accept Fellows receive additional compensation for expenses incurred in relation to their training programs.

Eligibility requirements include United States citizenship (or the declared intention of becoming a citizen), sound health, and an M.D., Ph.D., or an equivalent degree.

Selection of candidates is made by a Fellowship Committee composed of leaders in the fields of research and professional education. The designation "Fellow of The National Foundation for Infantile Paralysis" will be given to successful candidates.

Complete information concerning qualifications and applications may be obtained from: Division of Professional Education, The National Foundation for Infantile Paralysis, 120 Broadway, New York 5, New York.

Journal of the
AMERICAN MEDICAL WOMEN'S ASSOCIATION

EDITORIAL SECTION

THE FIRST BRANCH NUMBER

WITH THIS NUMBER of the JOURNAL we inaugurate a new series of special numbers, for which the Branches of the American Medical Women's Association will act as sponsors, and their members as authors.

First in the series rightfully belongs to Branch One, The Women's Medical Society of the District of Columbia. A special committee, under the chairmanship of Dr. Elizabeth Kittredge, and with the following members: Dr. Lois I. Platt, Dr. Josephine Renshaw, Dr. Carolyn S. Pincock, Dr. Charlotte Donlan, and Dr. Elizabeth Kahler, has collected outstanding articles of scientific, medico-legal, and historic interest.

The editors are grateful to Dr. Kittredge and her Committee for starting off this series with these fine papers, and trust that other branches will be stimulated to acquaint the Association with the work of their members in a similar fashion. Dr. Kittredge needs no introduction to this group who recall *Women in Medicine* of which she was the efficient editor; but to the newer members, who have not had the pleasure of knowing this genial personality, we are happy to add the following lines, contributed by one of her Washington colleagues.

ELIZABETH KITTREDGE, M.D.
Guest Editor

ELIZABETH KITTREDGE, beloved leader among medical women in the National Capital, was born in Massachusetts, completed her academic work at Vassar College, and later attended Columbia University, New York, where she met a young mechanical engineer, Herbert Whittemore, whom she eventually married. She received her medical degree from Johns Hopkins Medical School in 1922, interned at St. Elizabeth's Hospital, and then was physician at Vassar College. As Mr. Whittemore was on the staff of the United States Bureau of Standards, the family moved to the District of Columbia, and have ever since remained in this area. Their son is an electrical engineer and their daughter is completing her final semester at Antioch College.

Dr. Kittredge now claims that she has always been a "part time" medical woman. At present she works in the Maternal and Child Health Clinic of the District of Columbia Health Department.

For years Dr. Kittredge has been an active member of the American Medical Women's Association and we all recall with gratitude her devoted service as the editor of *Women in Medicine*, the first publication of the Association and the quarterly from which the current monthly JOURNAL has grown.

A descendant of the original colonist, Benjamin Kittredge, Elizabeth (like her contemporary kinsman, Benjamin Kittredge of the lovely Cypress Gardens, near Charleston, South Carolina) has carried on the family tradition of the good gardener. Her "green thumb" is famous among us. And there is in her manner something which encourages growth in patients and colleagues as well as in plants. May our culture boast many more women physicians with a "green thumb" like that of Elizabeth Kittredge!

LOIS PLATT, M.D.

Woman's Medical Society of District of Columbia

THE HISTORY OF BRANCH ONE OF THE A.M.W.A.

Elizabeth Kittredge, M.D.

IN THE SUMMER of 1909, Dr. Mary Parsons and her younger friends, Dr. Louise Tayler-Jones and Dr. Ada Thomas, wondered "if it would be possible to develop an organization of women physicians." Of the fifteen who attended that first informal meeting on October 30, 1909, at Dr. Parsons' office, only one is living, Dr. Patience Bourdeau-Sisco. Although she has made her home in Baltimore these many years, we see her at our joint meetings, and she has made a strong bond between the two cities.

Dr. Parsons was made chairman of the organization meeting and unanimously elected to the presidency of the new association in spite of her strenuous objections (Dr. Parsons was usually strenuous). Other officers were: Dr. Sophie Nordhoff-Jung, Vice-President; Dr. Emma Lootz-Erving, Secretary-Treasurer; and Dr. Mary O'Malley, Corresponding Secretary. At the first regular meeting when the constitution was adopted, Dr. A. Frances Foye and Dr. Elizabeth Sohon were among those who signed the register.

The minutes state: "Several having given their opinion, it was moved and carried that we form a club mainly for scientific purposes," that "meetings be limited to once a month for eight months of the year," and that "members present papers in alphabetical order."

The constitution stated: "Members shall be graduates in medicine in active practice who are members, or eligible for membership in the A.M.A. Meetings shall be held the second Tuesday of each month from October to May inclusive at 8:15 P.M." There were no dues. The constitution further stated: "Only such special assessment shall be made as will be necessary to defray the expenses of the Society." For a long time this was 25 cents but how often it was collected the minutes do not state.

This general plan of meeting has been followed through the years with surprisingly few changes. The alphabetical reading of papers has gone by the board. The second Tuesday has been changed to the first Tuesday, and only such outside cataclysmic events as Election Day, which fell on the same day as the 152nd meeting; New Year's Day, which sometimes comes on Tuesday; the influenza epidemic of 1918; and the second World War; have been allowed to modify this schedule. Somewhere along the line, refreshments crept into the picture, for at the 16th meeting, October, 1911, Dr. Stroebel reports that "The meeting adjourned to partake of toothsome repast provided." Some years later it was suggested by one of the older members that refreshments be limited to "one food, one drink," for by this time entertainment had become too competitive, and the older members decided to set a more moderate pace. The pattern of meeting at private homes with papers and refreshments has been a pleasant one. From time to time, other meeting places have been considered, and during the late war we accepted the hospitality of Doctors' Hospital, using the solarium. We now seem to be falling back into the friendly habit established at the first meeting, although there are few who have homes large enough for the increased attendance. Meetings of special interest have been held at such institutions as Takoma Park Sanitorium, St. Elizabeth's Hospital, and Children's Hospital.

Constitutions are never static, and ours has been no exception. In one of the constitutional changes in 1912, provision was made for the "suspension of members," but this was rescinded at a special meeting. One wonders why it was ever put in! It is not surprising to note that the dues have changed and the treasury has become of greater importance:

Treasurer's Report for May 4, 1915
47th Meeting

Balance	$3.03	
Rec'd during year	5.50	
		8.53
Expended for post cards	2.75	
Balance on hand May 4, 1915	$5.78	

Special assessments were levied for special occasions, such as flowers, and a "beautiful silver porringer for the cradle roll member, Charlotte Bruce Lyon." This, too, became so burdensome that another constitutional change in 1925 provided for dues of $2.00 and "no further assessments."

Minutes of the meetings hint of disagreements among the members, but the secretary was always discreet, and it is not told why one of our most important members once "refused to pay the assessment," later resigned, and still later was reinstated, played hostess, gave papers, and held national office.

Subjects covered by the papers, the case reports, and specimens constitute a picture of the changes in medical practice through the years. The first paper, October, 1909, was "A Slight Review of Orthopedics," by Dr. Emma L. Erving. Many specialties are now represented, but I think we have had no woman orthopedist in D. C. since that early day, and certainly none better. In a later paper she warned "Most joints are immobilized too long," a very modern point of view.

The subject of Dr. Parsons' presidential address in 1911 was Cesarian Section, "favoring its more frequent use." That fall, Dr. Parsons and Dr. Keith gave cases of the unusual incidence of malaria, a disease rampant in old Washington. Unsanitary conditions were reported to the Health Department. At the same meeting, Dr. Stroebel, who had been abroad, described the chastity belt seen in a museum in Paris.

In April, 1914, Dr. Thomas, on the basis of her own experience, spoke on "Intestinal Perforation in Typhoid Fever." Some years later she noted that there had been no cases of typhoid in the District for a year.

Distinguished guests were sometimes invited to speak. When Dr. Sophie Nordhoff-Jung was president, she invited Dr. Howard Kelly of Baltimore to come on January 6, 1914, with doctors from Philadelphia and "representatives of the local press." His subject was, of course, "Radium." In May of that same year Dr. Jung voiced the "earnest wish that the cause of cancer might be found in the next two years."

Dr. Jung was probably one of the best trained doctors in town and well known for her diagnostic acumen. Her interest in cancer took the very practical form of an award of $500 to be given each year to a worker chosen by members of the staff of the University of Munich in Bavaria. Dr. Jung took great pride in giving us the name of the winner of her prize before the public announcement was made. The first recipient was Dr. Fibiger of Denmark, who later received the Nobel prize.

In January, 1915, Dr. Lyon reported a paper read by "a Dr. Evans" on bacillus abortus which "is not pathogenic to humans, but is pathogenic to all animals."

In 1919, Dr. Ella Oppenheimer discussed immunization against diphtheria. The legal aspects of enforcing such immunization were considered, the final verdict being: "All thought it was a good thing to do when possible."

On February 6th, 1918, problems of the First World War were reflected in a program on Food Conservation, and the work of the American Women's Hospitals in Serbia.

These women were by no means stay-at-homes. At one fall meeting, where each member reported on the events of the summer, Dr. Anna Bartsch-Dunne had been in Vienna where she frequently went for post-graduate study, Dr. Nordhoff-Jung and Dr. Tayler-Jones had also been abroad, and Dr. Thomas had attended the Cabot Clinics in Boston.

Many causes, not strictly medical have been the concern of the Society. In fact, Dr. Parsons, in January, 1912, suggested "extra meetings to discuss subjects outside the scope of medical papers, yet of vital importance to the profession."

The first issue raised was "the use of certain books at the Library of Congress," and a committee was appointed. Reporting at the next meeting, Dr. Ada Thomas assured the group that Dr. Lyon "had inquired at Central and Business High Schools finding that none of these books are recommended by the faculty for the pupils' reading . . ." and from the Library itself, "Such books are listed in the usual manner . . . where it is known that very young people call for the books they are denied. Also children under 16 years of age are not allowed to get any books." The books remain unnamed in the minutes, and one wonders what they were. This must have been a lively meeting, for Dr. Thomas, always thoughtful, never impetuous, was "greeted with applause when she read a carefully prepared statement of authentic facts relating to this 'Horrible White Slave Traffic'." Being doctors, everyone had had some experience with illegitimacy and the venereal diseases. The discussion was full and varied.

At this meeting, too, Dr. Tayler-Jones asked for a special meeting to urge the appointment of a woman obstetrician at Garfield Hospital. The problem of internships and residencies for women has

been a matter of continuing concern to the Society. Petitions, letters, and personal appeals have been made to the D. C. Commissioners, and the Boards of various hospitals. When openings have occurred, the Society has tried to help find suitable candidates.

Early in the life of the Society, a committee on education was formed to provide speakers on medical subjects to lay groups. This was a most satisfactory activity. One year, forty-six such lectures were given by members.

Commissions for Women in the Army and Navy were finally granted in 1944, but the subject was not new. In July, 1922, it was noted that men students were being given time and money to serve in the R.O.T.C. An ally was found in Dean Borden of the George Washington Medical School. He advised women medical students to attend the lectures and urged the Surgeon General of the Army to grant the women the same status as men. A committee of three, Dr. Kate Karpeles, Dr. Ella Oppenheimer, and Dr. Amy Rule, was appointed by the Society to write to General Ireland ". . . making a strong and earnest plea for recognition of women medical students in the R.O.T.C." Dr. Karpeles who had served as a contract surgeon—a most unsatisfactory status—during the First World War was the leader in this fight. The pressure to include women in the R.O.T.C. backfired, however, for the women students were obliged to take the lectures and examinations with the men, but commissions were not forthcoming.

The Society was deeply concerned for professional recognition but declined to take part in anything that smacked of publicity. At a special meeting in 1913, "after free discussion," they decided to refuse the invitation of Miss Alice Paul to march as a group in the Suffrage parade planned for May 3, "although they all were in sympathy with the Equal Suffrage Movement."

Through the years social activities have never been neglected; banquets and dinners are mentioned frequently. The annual meeting with the Baltimore group, started by Dr. Sisco, has become a regular event. Such distinguished speakers as Dr. Maude Abbott, Dr. Esther Lovejoy, Dr. Catherine Macfarlane, and Dr. Priscilla White, have been guests of honor at these joint sessions. We have been hostess to the women of the A.M.A., our own National Association, the women of the Southern Medical Association, and other groups. Our annual picnics were held for years at the country home of Dr. Louise Tayler-Jones, and, more recently, Dr. Elizabeth Parker has been our hostess.

For the past few years, a new custom, that of paying special recognition to an outstanding member, has grown up. This spring we chose Dr. Anna Bartsch-Dunne. Not only has she been a leader in practicing conservative gynecology and proctology but she has established a scholarship fund at George Washington University School of Medicine in memory of her mother. Two awards are made annually, one to a woman student, one to an intern.

Interest and participation in the national association has always been a part of our program. In answer to a letter from the national in 1919, application blanks were offered "to any who might wish to join." Three of our members have held the office of president: Dr. Louise Tayler-Jones, Dr. Kate Karpeles, and Dr. Mary O'Malley. During her administration, Dr. Jones proposed and carried out the reorganization of the national association. She always took pride in three changes: the establishment of branches, life memberships, and the mid-year board meeting. In the revision of the constitution following these changes, it was moved by Dr. Foye, seconded by Dr. O'Malley, and passed in April, 1934, that "The Society shall be affiliated with the Medical Women's National Association. . . . and shall be known as Branch Number One of that Association . . ." There have always been one or more of our local members serving as chairmen or as members of the various committees of the A.M.W.A.

The life of a woman physician in Washington is a satisfactory one professionally. Women are admitted to all the medical schools; as a rule there are interns and residents in the hospitals; for those who are qualified, staff and courtesy appointments are available. With a few exceptions, the pioneering days are over. Now we plan to turn our attention to a more personal type of help for the younger women. Two committees are working together, "fellowship" and "big sister." Money formerly spent for flowers and porringers will be earmarked for a fund to be used as needed. Perhaps a small loan will be needed, perhaps illness will upset a budget. Rather new is the idea of a pool of books, instruments, even uniforms, which may be loaned to students. How many of us have a Sahli tucked away which a student must have but does not use after clinical clerkship days are over? Information about starting an office or other problems which defy classification will be available. All of us have profited from help from our older friends, and it is our wish that the Association, in a more formal way, pass on this help and good will to those entering the profession.

Women Doctors in Washington Today

A STATISTICAL SURVEY

Lois Irene Platt, M.D.

APPARENTLY, WOMEN DOCTORS in metropolitan Washington are normal career and family women. This statement is supported by replies to a questionnaire recently completed by 73.2 percent of the women doctors to whom it was submitted.

An attempt was made to reach every woman doctor in this area, whether or not she is engaged in medical work. A list of 267 names was compiled from the following sources: membership in Branch One, A.M.W.A. Women's Medical Society of the District of Columbia; official list of the Commission on Licensure of the Healing Arts Practice Act of the District of Columbia for 1951; mailing list of the District of Columbia Health Department; United States Public Health Service personnel office; District of Columbia Health Department personnel office; local hospitals; local medical schools (Deans' offices); various federal agencies; Medical Society of the District of Columbia; and names submitted by doctors returning the questionnaire.

However, the number of questionnaires distributed cannot be used as the total number of women doctors in the area, as it is reasonable to assume that several were missed. In view of the extent of the search made, it may be fair to estimate that there are between 250 and 275 women in metropolitan Washington who have an M.D. degree.

Among the 67 women who did not answer the questionnaire are 19 members of the local Women's Medical Society, Branch One, A.M.W.A. (all of whom either have been, or are now, in active medical work), and 13 residents or interns in local hospitals. Among the remaining 35 who failed to respond, several are known to be active in medical work. However, because these 67 did not respond, they cannot be included in this report.

Of the 200 responses, 11 were rejected because of duplication or residence outside the metropolitan area of Washington. The tabulations reported here are based on the 189 acceptable replies, and 258 is considered to be the number of local women doctors to whom the questionnaire was submitted.

NATURE OF THE POPULATION

The distribution of women doctors in the area by race, age, and nationality is shown in Table I.

TABLE I
NATURE OF THE POPULATION
By race, nationality, and age

Total answers tabulated	189
RACE	
White	172
Negro	13
Other (Chinese, Filipino)	4
NATIONALITY	
Foreign born	26
Native born	163
(Native Washingtonians, 18)	
AGE	
Under 35	63
35 to 60	107
Over 60	19

Negro women sent in 6.7 percent of the answers. Only 18 of the 189 women, about 10 percent of the total, were born in Washington. While 26, or 12 percent, were born outside the United States, only 2 of these foreign born women, 0.1 percent of the total, are not now citizens.

EDUCATION

The local women doctors were graduated from 54 different medical schools including 18 state universities, 22 other United States medical colleges, 2 schools no longer in existence, and 12 medical colleges outside the United States.* The 14 women who were educated outside the United States received their degrees in 9 different countries. Most of the doctors (95.4 percent) received their schooling in coeducational institutions. Although the District of Columbia boasts 3 fine medical schools, 70 percent of the local women doctors

The facts for this survey were gathered through the efforts of Branch One of the A.M.W.A. and its committee for this number of the JOURNAL *and were compiled by Dr. Lois Platt. Dr. Platt is a clinical instructor in surgery at George Washington University where she is doing research in the field of cancer cytology under the auspices of the American Cancer Society.*

TABLE II
LOCAL MEDICAL SCHOOL POPULATION

Medical College	All Students		Women Students			
	Graduates 1951	Four Classes 1950-51	Graduates 1951		Four Classes 1950-51	
	No.	No.	No.	%	No.	%
Howard[1]	66	288	10	15.1	29	10
George Washington[2]	72	331	7	9.7	16	4.8
Georgetown[3]	104	364	5	4.9	25	6.9
Total	242	983	22	9.1	70	7.1

[1]Howard University College of Medicine; [2]George Washington University School of Medicine; [3]Georgetown University School of Medicine.

were educated in schools outside the District of Columbia. Thus, it can be said that Washington medical women are a group with educational background representing every section of this country and a fair sampling of the rest of the world.

All three of the local medical colleges accept women students. The current school populations are shown in Table II, which gives the total numbers and percentages of women students.

Since the founding of its medical school in 1868, Howard University (a federal institution) has never discriminated against prospective students on the basis of either race or sex. In both the graduating class of this year and the class entering this fall at the Howard College of Medicine women are found in a ratio of one to every seven (total) students. This is approximately the ratio in the total number of physicians listed in the official list of doctors licensed to practice in the District of Columbia. It is interesting to note that in the one local school which has never discriminated against women applicants, the percentage of women students closely approaches the local and the national ratios of practicing physicians. Locally, the 1951 percentage of medical students who are women (7.1 percent) is almost exactly that (7.2 percent) of the nation.[1]

The first woman to graduate from a local medical school was Mary Dora Spackman, a local resident who graduated from Howard's second medical class, 1872, with seven other students. George Washington University, then the Columbian University Medical Department, graduated its first woman doctor 15 years later (1887), when Clara Bliss Hinds received her degree. Georgetown University, which only recently (1947) opened its doors to women students, granted the first M.D. degree to a woman in 1949.

Practice

In regard to type of medical work, 157 women (82.6 percent) are in active full time medical practice; 18 are in part time practice; and 14 are not in practice. Table III summarizes the answers concerning the extent and type of medical work. It is obvious that the numbers in the two columns in Table III do not add up to the totals doing full or part time medical work. Each woman was classified according to her own evaluation of how she spends her time. For instance, she might rate herself as being in medical work full time consisting of two or more part time jobs. Or she might count two or more part time jobs as totaling only part time work in the field. Of the 18 women who consider themselves in practice part time, 3 are over 60 and might as well have listed themselves as partially retired; 12 are young mothers with young children; 3 gave no reason for doing only part time medical work. One of this last group is also a full-time professor of psychology, an activity which she classed as non-medical.

TABLE III
EXTENT AND TYPE OF PRACTICE*

Type of Work	Extent	
	Full Time	Part Time
Total in medical work	157	18
Private	58	27
Institutional	3	20
Federal Agency	44	2
District Agency	11	5
State Agency	3	1
Research	13	3
In non-medical work	1	2

*For explanation see text.

*Foreign medical colleges: University of Vienna and Innsbruck University, Austria; McGill University and Universities of Toronto, Canada; Women's Christian Medical College of Shanghai and Lin Nan Medical College of Canton in China; University of Tartu in Estonia; Ruprecht University, Germany; Edinburgh University, Great Britain; University of St. Thomas, Philippines; University of Basle, Switzerland; Istanbul University, Turkey.

Of the 14 women not in practice, only 3 can be classed as not having adequately used their medical education. All three are married and have children; two of these did active medical work for five or more years. Only one woman out of the 189 never practiced! The remaining 11 not now in active medical work are grouped as follows: retired, 4; foreign born and educated and not yet licensed, 2; wife* of an army officer recently moved to District of Columbia, 1; illness, 1; young mothers (who will probably practice again), 3.

Specialties

Slightly over one-fourth of the women (50 women, 26.2 percent) have attained the official rating of specialist by passing the specialty board in their chosen field (Table IV). Practice limited to a special field was listed by 106. It will be noted that in Washington the number of certified women physchiatrists exceeds those certified in any other specialty; pediatricians are a close second; and pathologists are third. It was surprising to some who reviewed the figures in Table IV that obstetrics is not first, since most women claim that, whether they choose or not, they are called upon to do a high volume of obstetric and gynecologic work. But here tabulated are only those women who have had sufficient interest and opportunity in a given specialty to achieve certification by the specialty board in that field.

TABLE IV
SPECIALTIES

Total certified in a specialty	50
Dermatology and Syphilology	2
Internal Medicine	3
Obstetrics and Gynecology	3
Ophthalmology	2
Otolaryngology	2
Pathology	6
Pediatrics	12
Physical Medicine and Rehabilitation	1
Preventive Medicine	2
Psychiatry	14
Public Health	2
Radiation Therapy	1

Marital Status and Offspring

Since 66 percent of the women have married (Table V), it can scarcely be argued that a medical career precludes matrimony. In fact, marriage is 20 percent more frequent among Washington's women doctors than among all gainfully employed women throughout the United States.[2] In the local area, the percentage of women doctors married is slightly higher than the percentage of married women in the general population of Washington (59.5 percent and 54.7 percent, respectively).[3]

*Since the preparation of this report, the doctor listed here has accepted a full-time federal agency clinic position.

TABLE V
MARITAL STATUS AND OFFSPRING

Marital Status	
Married*	113
Widowed	6
Divorced	7
Single	63
Over age 35	39
Under age 35	24
Offspring	
Number with children	91
Number without children	27
Total number of children	181
Average number of children	2

*51 are married to medical men.

In attempting to evaluate the relationship between offspring and practice, it is interesting to note that only 13 of the 91 doctors with children have been out of practice 5 or more years. There are 28 women who have 3 or more children. Of these, 8 have not been out of medical work for a total of 1 year; 16 are now doing full-time practice; 7 are now in medical work part time.

As elsewhere in the nation,[2] the trend among Washington women doctors seems to be toward smaller families. It is, of course, foolish to attempt to translate such small numbers into rate-terms comparable to those used by census statisticians. Hence, no attempt has been made to compute the birthrate. But with 91 women having an average of 2 children each, their family units suggest the story-book size of the "typical American family."

Hospital Affiliations

Hospital connections are frequently cited as an index of activity among doctors. There were 426 hospital affiliations listed by 104 of the women answering the questionnaire. Correction of the figures for the 8 interns and 26 residents in hospitals shows that 70 women have 392 hospital privileges or an average of 5 or 6 per practicing physician. The 71 with no hospital affiliations are largely accounted for by the women distributed among the government agency and research workers.

Teaching Appointments

Medical school teaching appointments are held by 61, nearly one-third of the local women doctors (31 percent), and professorial rank has been attained by 13 or 6.7 percent. This number applies only to those who hold appointments on a medical school faculty, although many others are probably engaged in teaching activities, especially in connection with their hospital staff appointments.

Medical Organization Membership

The total number of memberships held by women in medical organizations is 464; total offices held in these organizations, 55; the number of women holding office is 25 (12 percent). Not all women doctors are joiners; 55 women (30 percent) did not belong to any medical organizations. On the other hand, 25 women (12 percent of the total) had memberships in more than 5 organizations.

Professional Writings

Some of the local women doctors are prolific writers. The total number of papers by women doctors of the area which have appeared in journals in the last 5 years was 211, the number of women who had had publications was 41, and 13 women had over 5 publications. One woman sent a bibliography of 61 titles, 11 of which had been published within the last 5 years. Over one-fifth (21.5 percent) of the women have had at least one paper in a medical journal in the last 5 years, while 6.6 percent have averaged one or more such publications a year during the five-year period.

Miscellaneous Information

Many other items to characterize the Washington woman doctor can be gleaned from the answers to the questionnaire. To cite a few: one is the director of a state mental hygiene clinic. A research worker in public health administration writes health education bulletins for lay consumption. One is licensed to practice in five states. A formerly very active woman has been in part-time medicine for the last five years because of the illness of her husband. A retired woman is still active in three medical societies. One, aged 61, fills four very active part-time jobs. A Negro woman, aged 80, is in full-time private practice, has given papers annually in four organizations for 50 years, and has acted as secretary in one organization for 30 years. One is the Assistant Superintendent of Gallinger Municipal Hospital. Another woman doctor holds two law degrees. A Negro resident, aged 28, already has had a paper published in a national medical journal. One woman is an associate editor of a specialty journal; and another serves on the board of book reviewers for the United States Quarterly Book List. And then there is the grand old lady who retired from her Washington practice to a small town before World War II, but, finding herself needed by the doctorless community, cared for her neighbors while the men were at war, and, at the age of 80, passed the Pennsylvania State Board Examinations.

What it means for an established doctor abroad to become reestablished in this country is illustrated by a woman who came here from Turkey four years ago. She was graduated from Istanbul University Medical School in 1939, and continued her training in hospitals, being certified by the Specialty Board of Obstetrics and Gynecology there in 1943. From 1944 to 1947 she did private practice in Ankara with her own private 20-bed hospital for surgery and obstetrics, and also rose to the position of second-in-charge in Ankara's Model Hospital. She is married, has one child, and has done full-time medical work ever since graduation, except for six months for confinement and delivery. She is now doing a full-time residency in obstetrics and gynecology at a local hospital.

Federal and District agencies employ qualified women doctors who apply for appointment. In the District Health Department there are 128 physicians, 22 (17.2 percent) of whom are women. Most local hospitals now accept women on the house staff for training. Eight such hospitals gave us names of 47 women interns and residents.

Comparison between this study and similar studies conducted in other localities are not attempted here. However, a number of such papers are listed in the bibliography [4,5,6,7,8,9,10], perhaps with the hope that someone (better qualified than the members of the committee conducting this local survey) may be able to compile a more general report on the use to which women doctors put their medical education. The committee felt that the trends indicated by this study might be cited as encouragement to qualified young women who want to study medicine. The facts given by the local women doctors seem to indicate that the District of Columbia with its surrounding metropolitan area in Maryland and Virginia has attracted an interesting and hard-working group of women physicians.

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A. FRANCES FOYE, M.D.

DR. FOYE sums up her life very simply in one sentence: "Since September, 1898, when I hung out my shingle, I've been constantly in the general practice of medicine in Washington, D. C." Once she was abroad for six months, "for pleasure only," and she has taken a few vacations, but, day-in day-out, morning, noon, and night, she has been, and still is, at the service of the sick who need her. In the nation's capital many important people have come to her office, foreign envoys (their wives and their children), "cave dweller" Washingtonians, and a president's wife and family, but *not* the President. He preferred to stick "to his own blacksmith."

Born in Honeyoe, Ontario County, New York, Dr. Foye came to Washington for a visit when a young girl. Washington appealed to her; so did the practice of medicine; so back she came, went to Sidwell Friend's School, and entered Howard University Medical School, graduating in 1898.

In September she started practice, and her first three patients were men. A woman doctor was, of course, still a novelty, and a neighboring parrot greeted her as she started out with a cheerful, "There goes the doctor!"

Dr. Foye's manner of getting about is a history of transportation. First she walked, rode a bicycle, or used the street cars. Then her horse, Charley Fox, became almost as well known as the doctor herself. Progress, however, brought, in succession, an electric Rauch-Lang, the inevitable Model T, and a long line of modern cars.

Dr. Foye has done most of her work at Garfield and Sibley Hospitals. Her latest triumph was the diagnosis and delivery of triplets, last September.

She is a charter member of the Woman's City Club, served a term as its president, and has always been active in its affairs. When Mme. Curie came to this country the club gave $250 and a patient of the doctor's matched it with another $250, making the total of a $500 contribution for the radium so urgently needed.

Dr. Foye is a member of the Medical Society of the District of Columbia, and a fellow of the American Medical Association. When the Medical Society built its present building, she was on the building committee. A charter member of the Woman's Medical Society, she made the motion to have the society become Branch One of the national society when it was reorganized. She has served on many committees of both societies.

Dr. Foye has always shown a keen interest in the younger medical women and has helped many of them in many ways to get started in practice. Her enthusiasm, sympathy, and ability to solve problems have helped many over a tight place.

Dr. Foye is a beautiful woman. Her hair is now snowy white, and many there be who envy the lilt of her carriage and the sparkle in her eye. She has a gracious and charming manner, and her conversation is witty and entertaining. In the present day of specialization she is the finest example of the family physician.

ELIZABETH KITTREDGE, M.D.

MAY DAVIS BAKER, M.D.

DR. MAY BAKER has been characterized by her younger friend, Dr. Foye, as ". . . one brilliant woman filled with common sense and kindness itself toward her fellows." She is a "Grand Old Lady of Medicine," and Washington counts her as one of its own. Anyone, still lame from a broken ankle, who will come from Pennsylvania to Washington to give us her ideas on the treatment of diabetes is still a member of our Association.

Dr. Baker was born in Ohio, in 1866. While teaching in Kansas, she met and married Arthur B. Baker who was County Supervisor of Schools. Two children had died in infancy, and when Mr. Baker came to the Smithsonian in Washington as Assistant Director of the National Zoological Park, May decided to study medicine. She wished to be better prepared to care for her family if they should return to the West. Not only was she interested herself, but she persuaded her older sister, Carrie, to enter medical school.

Dr. Baker entered Columbian College (now George Washington), but women were not too welcome there at that time. She then went to Howard. Howard National University had been established by the government without any restrictions as to sex or race, and a number of our women doctors found that, of the few schools available, it gave the best training. Howard is now better known as a Negro college, but there are still white students enrolled in some of its departments. From the very first, there have been women in the classes of the Medical School.

Dr. May Baker graduated in 1896 and received her license to practice that same year. Examinations for license to practice were not established until some years later, so she never had to take the examinations in the District.

May Baker carried on a busy city practice for nearly fifty years, then decided it was time to stop. She gave up her office and her home and went to Pennsylvania to be near her son, Dr. Arthur G. Baker. These were the war years when every available doctor was needed at home as well as in the service. Being a physician, she could do nothing but take up her work again, as people kept coming to her. After the war, at the age of 80, she took and passed the Pennsylvania State Boards, no mean achievement.

Dr. Baker and Dr. Foye represent the fine group of women, not the earliest pioneers, but those post-pioneers who came a little later and, by their enthusiasm, high professional standing, and willingness to put up with or overcome the very real prejudices that are now so nearly gone, helped put women as doctors on a plane of dignity and respect from which we have all reaped the benefit. Sometimes it seems more dramatic to blaze a trail, but a new philosophy needs steady, hard, and faithful work; Dr. Baker and Dr. Foye can view the present-day acceptance of the woman doctor as their reward.

ELIZABETH KITTREDGE, M.D.

These Were The First

Elizabeth Bass, M.D.

Dr. Mary Harris Thompson (1829-1895), graduate of the Woman's Medical College of Pennsylvania, founder in 1865 of the Mary Thompson Hospital, Chicago, a hospital built for women, by women, and staffed by women, is considered to be "the first woman surgeon who performed capital operations on her own responsibility" in the United States of America.

Dr. S. Satthianadham was the first Indian woman to graduate from Madras Medical College, which was the first medical school in India to open its doors to women (1894). She died at the age of 32, and scholarships and medals in her honor have been given at the school to perpetuate the name of this pioneer woman physician.

Dr. Sara H. Stevenson was the first woman admitted to the American Medical Association (1876).

Dame Louisa Aldrich-Blake, surgeon graduate, University of London, was the first woman to obtain the degree of Master of Surgery in England. She was Dean of the London School of Medicine for Women and one of the first women to practice general surgery. She died in 1926.

Dr. Emiline Horton Cleveland (1829-1878) was the first woman ovariotomist in Philadelphia (1872). Later she was Dean of the Woman's Medical College and one of the early advocates of bedside training. She established a nurses training course at the Woman's Hospital of the Female Medical College where she was the first resident.

Captain Marion C. Loizeau, graduate of Cornell University Medical School, 1931, and a diplomate of the National Board of Medical Examiners in 1933, was the first woman physician to hold a commission in the Army Medical Corps in the European Theater of Operations.

Dr. Ella Blaylock (1860-1933) was the first woman to obtain a degree in Surgery in Quebec (1887), from Queen's University.

Dr. Sara Welt-Kakels, a graduate in 1885 of the University of Zurich, and Fellow of the New York Academy of Medicine (1897), was the first woman pediatrician to become a member of the staff of Mount Sinai Hospital, New York (1887).

Dr. Esther Pohl Lovejoy was the first president of the Medical Women's International Association, in which capacity she served five years. She was appointed Health Officer of Portland, Oregon (1907-1909), the first woman to receive such an appointment in a city of comparable size.

Dr. Elizabeth Riefsnyder opened the Woman's Union Missionary Hospital in 1883 in Shanghai and performed the first operation by an American woman physician on a Chinese woman for ovarian cyst.

Dr. Helen Octavia Dickens, gynecologist, was the first Negro woman physician admitted to the American College of Surgeons (1951).

Dr. L. Rosa Gantt (1875-1935) was the first woman physician to practice in Spartanburg, South Carolina, where she practiced for 32 years. A graduate of the first class that admitted women in the Medical College of the State of South Carolina, Dr. Gantt was a fearless leader in public health and civic work, established traveling health trucks in mountainous regions, and in the first World War was commissioned by the U. S. Department of Commerce as Medical Examiner of Air Pilots. In 1932 she was president of the Medical Women's National Association (now the A.M.W.A.).

Dr. Maude Abbott (1869-1940) was the first woman elected to membership in the Medico-Chirurgical Society of Montreal (1899). In the same year she was appointed to the curatorship of McGill's Medical Museum. She was instrumental in establishing the International Society of Medical Museums and her "Atlas of Congenital Cardiac Disease" is a classic text.

It's Wonderful . . .

The prompt and gratifying response we have had from you on the Survey! Already the return is 33 percent and our great hope is that it will go even higher. It will —if those of you who have not yet answered the questionnaire will fill it out and return it to us in the prepaid envelope.

And you who are, unfortunately, not members of the Association—won't you please complete the questionnaire you have received and send it to us today? We value YOUR answers as well as those of Association members because you, too, read this JOURNAL with a critical and appreciative eye.

You will all be pleased with the results of the final tabulation which will be published in these pages after the mailing has been completed. So again we ask the cooperation of all who are just now receiving the survey—may we count on you?

MEDICAL WOMEN'S INTERNATIONAL ASSOCIATION

All members of the American Medical Women's Association are invited to attend the scientific sessions and the social affairs arranged for the Council meeting of the MWIA. The meeting will be held next September in or near Paris; the exact time and place will be announced next month.

Under consideration is a plan of travel which includes transportation to and from the meeting and, in addition, a two weeks tour through Germany, France, Switzerland, and perhaps other countries, either before or after the meeting. Visits to scenes of medical as well as travel interest will be arranged. The tour need not be restricted to members of AMWA or to women physicians.

It is hoped that a large number of AMWA members will attend the meeting and join the group. If interested, please write for further details to the Business Manager, J.A.M.W.A., Suite 210, Two Lexington Avenue, New York 10, N. Y.

IMPORTANT ANNOUNCEMENT RE THE DIRECTORY

The directory of members is now being prepared for printing. Was the listing of your name, address, and type of practice in the 1949 Yearbook correct? If you became a member since that Yearbook was published, was your name, address, and specialty correct as printed in the listing under New Members appearing in the JOURNAL? If any corrections are necessary, please send them before December 31, 1951 to Directory, J.A.M.W.A., Room 210, Two Lexington Avenue, New York 10, N. Y.

No changes in or additions to the Directory will be made after December 31, 1951.

* * * *

We regret that News of Medical Women, Book Reviews, and Current Publications, have had to be omitted from this number of the JOURNAL because of lack of space.

—Ed.

EDITORIAL FORECAST

December, 1951

This is the Fourth Annual Number devoted to the Woman's Medical College of Pennsylvania, the material being supplied by members of the staff, with Dr. Carmen C. Thomas as Guest Editor. Among the articles being presented are:

"ACTH and Cortisone in Ocular Disease," by Grace Nachod, M.D., Clinical Instructor in Opthalmology.

"Dysfunctional Uterine Bleeding," by Sarah Sykes, M.D., Resident in Gynecology.

"The Cancer Problem," by Machteld Sano, M.D., Associate Professor of Pathology.

"Cystic Fibrosis of the Pancreas: A Case Report," by Benjy Brooks, M.D., formerly Resident in Pediatrics.

"Recent Advances in Dermatology," by Carmen C. Thomas, M.D., Sc.D. (med.), Professor of Dermatology and Syphilology.

"Ten Year Survey of Stillbirths and Neonatal Deaths, Hospital of Woman's Medical College," by Anne H. Pike, M.D., Clinical Assistant in Gynecology and Obstetrics.

"Role of the Student Health Service in a Medical School," by June Klinghoffer, M.D., Co-Director of Student Health.

In addition there is a symposium on medical education with Irene E. Maher, M.D., Assistant Dean, discussing "Pre-Professional Education"; and Marion Fay, Ph.D., Dean of Woman's Medical College, "Trends in Medical Education."

And Dr. Edith Millican, in "Medical Women in Foreign Missions," tells the story of these valiant medical missionaries, the first of whom, Dr. Clara Swain, was a graduate of Woman's Medical College.

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Burgess, T. S.: *Jour. Med. Assn. Georgia*, 37:44, Feb., 1948.

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**Gosselin, George A., M.D.*
Neurology and Physiology in Functional States
Connecticut State Medical Journal
15: 109-113, (February) 1951

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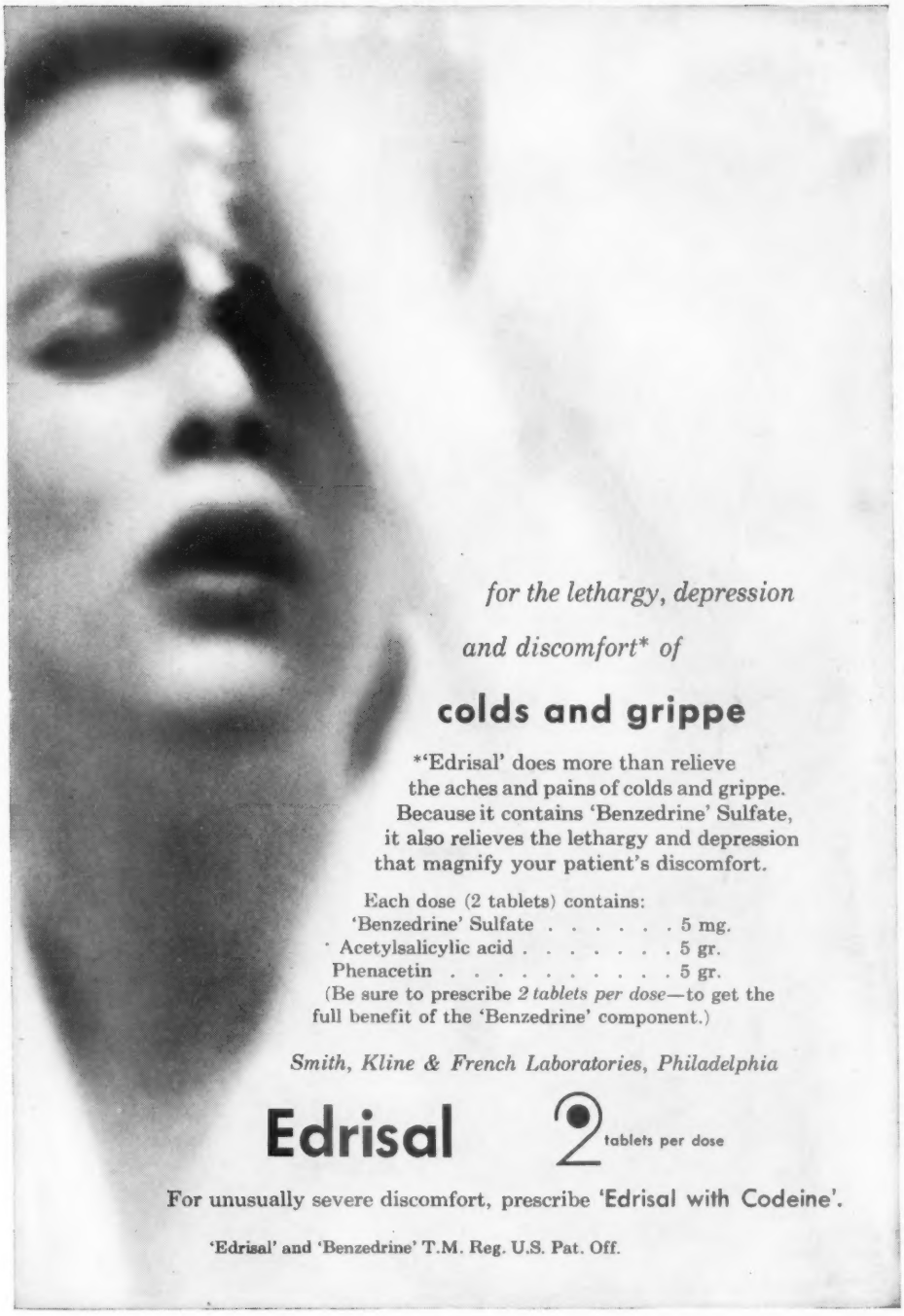

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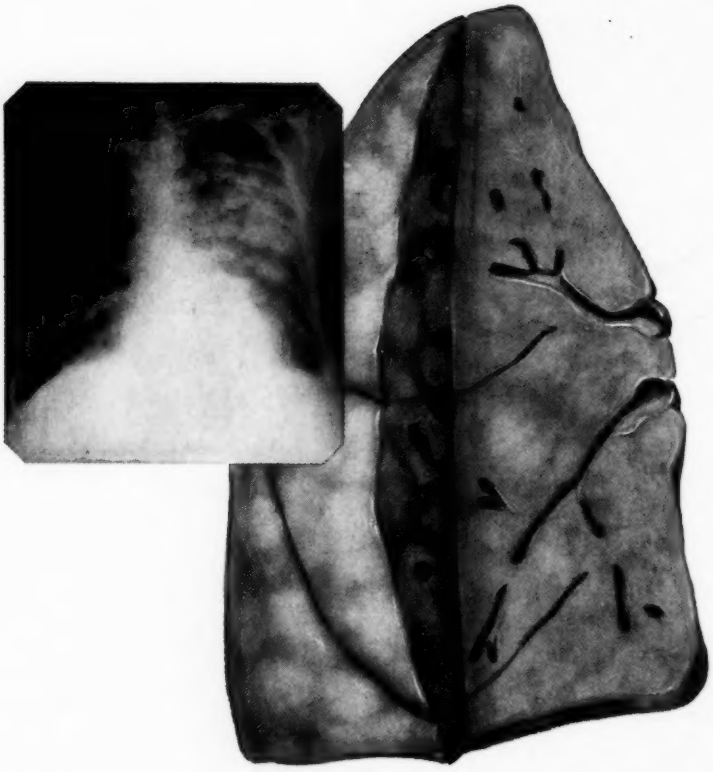

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Posterfield, T. G., and Starkweather, G. A.: J. Philadelphia General Hosp. 2:6 (Jan.) 1951.

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